

Press conference II

UEGW 2011

Monday, 24 October 2011, 13.00 h

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Room 201 (next to the Press Centre)

Topics:

- New European guidelines set quality standards for screening colonoscopy
- Latest developments will “dramatically change” the management of Barrett’s oesophagus and oesophageal cancer
- Patterns of gut bacteria could help improve health and well-being
- Evidence emerges that colon cancer may be a bacteria-related disease

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PRESS RELEASE

Latest developments will “dramatically change” the management of Barrett’s oesophagus and oesophageal cancer

(Stockholm, 24 October 2011) The results of several major studies assessing novel approaches to the detection and treatment of Barrett’s oesophagus and oesophageal cancer will be presented at this year’s United European Gastroenterology Week (UEGW) in Stockholm, Sweden. According to Professor Jacques Bergman from the Academic Medical Centre in Amsterdam, Netherlands, speaking to journalists at a UEGW press conference at the meeting, these results will have a major impact on the way patients are diagnosed and managed in the future. “Some of the finest research in the field of oesophageal cancer and the management of Barrett’s oesophagus is being presented at this meeting,” he said. “This research will dramatically change the way we screen for Barrett’s patients, the way we identify those at risk of progressing to cancer, and the way we treat early cancers in these patients.”

What is Barrett’s oesophagus?

Barrett’s oesophagus is a condition that affects the lower section of the oesophagus nearest the stomach. The cells (squamous cells) lining this part of the oesophagus gradually change and become more like those lining the stomach (columnar cells) – usually as a result of the long-term reflux of stomach acid into the oesophagus. Although the changed cells of Barrett’s oesophagus are not cancerous, they are at increased risk of turning cancerous over time, leading eventually to oesophageal adenocarcinoma.

According to Prof. Bergman, while still relatively rare, the incidence of oesophageal adenocarcinoma has increased six-fold in the last 40 years – an increase unsurpassed by any other cancer in the Western world. “Unfortunately, most oesophageal cancers are still diagnosed at an advanced stage where the prognosis is extremely poor,” he told journalists.

New developments in surveillance

Most patients diagnosed with Barrett’s oesophagus undergo regular endoscopic surveillance in order to detect early cancerous cell changes (neoplasia) at a curable stage. The problem, said Prof. Bergman, is that most Barrett’s patients remain undiagnosed and are not part of a surveillance programme. Large-scale endoscopic screening for Barrett’s oesophagus is not considered cost-effective and is associated with a relatively low yield, since the annual cancer progression rate is as low as 0.5%. “However,” said Prof. Bergman, “recent

developments in this field, such as the use of trans-oral sponge cytology and molecular markers for cancer progression, open the very real possibility of large-scale and cost-effective screening for Barrett's oesophagus in patients with known risk factors for this condition (e.g. white ethnicity, older age, obesity, and long duration of gastro-oesophageal reflux disease symptoms such as heartburn)."

Trans-oral sponge cytology is a new technique that involves swallowing a small "sponge" attached to a string – called a Cytosponge. The sponge collects cell specimens from the Barrett's region of the oesophagus and is withdrawn using the string for laboratory processing. "This allows the detection of Barrett's patients without the need for endoscopy and has the potential to identify individuals who otherwise might progress to advanced cancer, with a chance of early diagnosis by endoscopic means," he added.

A variety of molecular markers for Barrett's cells at risk of progressing to oesophageal cancer are also under investigation. According to Prof. Bergman, these markers can be found in brush cytology specimens from Barrett's segments, thus reducing the sampling errors that are inevitably associated with biopsies. "Patients at risk might then be treated prophylactically, whereas surveillance may be stopped altogether in low-risk individuals," he explained. "Although these tools are not yet commercially available, they are expected to change the management of Barrett's patients considerably in the near future."

New developments in treatment

Cancer of the oesophagus has traditionally been treated by removal of the oesophagus, which is a major and complex procedure that is frequently associated with serious complications. Newer treatments such as laser therapy, photodynamic therapy, radiofrequency ablation and endoscopic resection are designed to remove just the abnormal cells from the lining of the oesophagus – thus sparing the oesophagus.

"Multicentre European studies show that the treatment of early neoplasia in Barrett's using a combination of endoscopic resection and radiofrequency ablation results in the complete removal of the Barrett's segment in almost all patients," said Prof. Bergman. "The final results of a major European study on the endoscopic treatment of Barrett's-associated neoplasia are being presented at this meeting and the results are truly spectacular."

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PRESS RELEASE

Patterns of gut bacteria could help improve health and well-being

(Stockholm, 24 October 2011) Scientists have moved one step closer to being able to predict an individual's response to diet and medications based on an analysis of their gut bacteria. Studies published in the prestigious journal *Nature* show that human populations can be differentiated by their intestinal microbes, with individuals grouped into just three "enterotypes" irrespective of where they live, their health, or their age. Enterotypes – which have been likened to blood types – are defined by characteristic populations of bacterial species and the functions they perform, and it is hoped a better understanding of bacterial patterns may have important medical benefits.

"The results from these recently-published studies may well lead to the discovery of microbial properties that correlate with human health and allow classification of groups of people that respond differently to diet or drug intake," said Professor Dusko Ehrlich from the Institut National de la Recherche Agronomique in Jouy-en-Josas, France, speaking at a press conference at the United European Gastroenterology Week (UEGW) in Stockholm, Sweden. "Intestinal bacterial genes may also prove to be very useful as biomarkers for disease, and could eventually help to indicate an individual's overall health status."

Intestinal bacterial genes: more than 3 million identified

In March 2010, *Nature* published the first comprehensive catalogue of human intestinal bacterial genes, delineated by the MetaHIT (Metagenomics of the Human Intestinal Tract) consortium using stool samples from 124 individuals from Denmark and Spain.¹ Over 3 million microbial genes were sequenced and characterised. During the study, it was discovered that gut bacteria encode 150 times as many unique genes as the human genome itself, and that each individual harbours at least 160 bacterial species out of a total of around 1,000 species that predominate in the gut.

"We know that gut microbes have a profound influence on human physiology and nutrition and are crucial to human life," explained Prof. Ehrlich. "If we are ever to exploit the potential of these microbes to the benefit of human health and well-being, we must understand the content, diversity and function of the microbial gut community. This study moved us one major step further forward in this respect and paved the way for future studies assessing the association between microbial genes and human phenotypes."

Unique bacterial patterns revealed

Moving forward, researchers then used the same genetic analysis technique – called metagenomics – to study populations of bacteria in stool samples from 22 people in Denmark, France, Italy and Spain and combined the results with existing data from cohorts in Japan and the USA.² Their analysis revealed three well-defined enterotypes, determined by the relative abundance of different networks of bacterial species in the gut. Overall, the bacterial species *Bacteroides*, which is generally known for breaking down carbohydrates, was the most abundant species, accounting for about 12 percent of all bacteria found and predominating in enterotype 1. *Prevotella* species, which help to metabolise proteins, were abundant in enterotype 2, and *Ruminococcus*, which help to break down mucins and sugars, predominated in enterotype 3.

While the type of bacteria present in the gut did not appear to be related to any specific host characteristic, this was not the case for the bacteria's function. For example, the presence of bacteria capable of breaking down starch appeared to increase with age, while men seemed to carry more bacteria capable of synthesising the amino acid aspartate.

“Although these data are preliminary and need confirmation, we are excited by their potential to improve human health,” said Prof. Ehrlich. “Since we know that gut bacteria help to metabolise drugs and change the absorption behaviour of human cells – and it is likely the three enterotypes do so in different ways – it is possible that we could optimise the use of drugs and diet based on an individual's enterotype.”

Knowledge of enterotypes may also help with the development of techniques to restore healthy gut communities and could eventually be used for diagnostic and prognostic purposes.

References

1. Qin J, Li R, Raes J, et al. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* 2010; 464: 59-65.
2. Arumugam M, Raes J, Pelletier E, et al. Enterotypes of the human gut microbiome. *Nature* 2011; 473: 174-80.

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PRESS RELEASE

New European guidelines set quality standards for screening colonoscopy

(Stockholm, 24 October 2011) Higher and more reproducible standards for bowel cancer screening colonoscopy are on the horizon thanks to the development of new European quality guidelines. The guidelines (coordination: Dr Bjorn Rembacken), which will soon be published by the European Society of Gastrointestinal Endoscopy (ESGE) – an affiliated member of the United European Gastroenterology Federation (UEGF) – propose thresholds for acceptable colonoscopic practice, with the aim of guiding countries setting up organised screening programmes. Speaking at a press conference at the United European Gastroenterology Week (UEGW) in Stockholm, Sweden, Professor Thierry Ponchon from E. Herriot Hospital, Lyon, France, told journalists he believed the new guidelines would have a significant impact on clinical practice by helping to raise standards. “Colonoscopy is fundamental to most bowel cancer screening programmes and the success of these programmes requires the prompt provision of a high quality colonoscopy service,” he said. “To minimise risk and maximise benefits, all countries providing these services must put robust quality assurance frameworks in place.”

Screening for colorectal cancer

Many countries in Europe are now introducing organised screening programmes for colorectal cancer based on the faecal occult blood (FOB) test, which is the only screening method currently recommended by the European Union. A positive result on the FOB test usually prompts referral for colonoscopy to screen for polyps, non-polypoid lesions and colorectal cancers. Unfortunately, bowel cancer screening colonoscopy is not without risk, with a small potential for harm caused by oversedation, colonic perforation, bleeding resulting from polypectomy, or surgical complications following resection of benign or malignant tissue. This, said Prof. Ponchon, was the reason why there was a pressing need for quality indicators and quality assurance standards for screening colonoscopy.

“In developing the Quality in Screening Colonoscopy Guidelines¹, our objective was to outline the key indicators of colonoscopy performance that should be agreed and monitored within an organised screening programme,” he told journalists. “By doing so, we believe that all patients referred for colonoscopy screening will be able to expect consistently reproducible high standards.”

New standards for screening colonoscopy

The new guidelines outline strict quality standards for 15 issues ranging from cleaning and disinfection of equipment to bowel cleansing, colonoscope withdrawal time and acceptable perforation rates (Table 1). National Screening Boards are advised to set minimum standards for the level of experience required for screening colonoscopists and to ensure that all screeners are of sufficient calibre. These standards will be presented during the **annual ESGE “Quality in Endoscopy” symposium** dedicated to colonoscopy in 2012 (Berlin, 3-5 May, programme on ESGE website) and co-organised with ESDO.

Table 1. ESGE quality standards in screening colonoscopy

Quality assurance item	Proposed standard
1. Cleaning and disinfection	Routine microbiological testing no less frequent than 3-monthly
2. Consent and withdrawal of consent	<5% of cases to decline colonoscopy on the day of the procedure or withdraw consent during the procedure
3. Experience of screening colonoscopist	To be agreed by Screening Boards
4. Bowel cleansing	At least 90% of examinations to be rated as “adequate” bowel cleansing or better
5. Sedation, analgesia and comfort	No more than 1% of patients should become hypoxic (saturation <85% for >30 seconds) or for other reasons require administration of a reversal agent
6. Unadjusted caecal intubation rate	At least 90% unadjusted caecal intubation rate
7. Adenoma and cancer detection rates	To be agreed by Screening Boards
8. Colonoscope withdrawal time	A minimum of 6 minutes in at least 90% of purely diagnostic examinations
9. Polyp retrieval rate	≥90% of resected polyps should be retrieved for histological analysis
10. Significant interval lesions	To be agreed by Screening Boards
11. Specialist referral for removal of larger polyps	To be agreed by Screening Boards
12. Tattooing of larger polyps and cancers	Tattoos should be placed following removal of all polyps ≥2cm
13. Unscheduled readmissions	To be agreed by Screening Boards
14. Perforation rate	<1:1000 perforations complicating diagnostic or therapeutic examinations should require surgical repair
15. Bleeding rate	<1:1000 cases of bleeding should require surgical intervention

“These guidelines should not only help to set high standards for screening colonoscopy, but they can also assist with auditing and performance improvement,” said Prof. Ponchon. “We hope the guidelines will be adopted by all European countries that have, or are planning, organised bowel cancer screening programmes.”

¹The ESGE quality in screening colonoscopy guidelines will soon be published in the journal Endoscopy.

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PRESS RELEASE

Evidence emerges that colon cancer may be a bacteria-related disease

(Stockholm, 24 October 2011) Researchers in France have shown for the first time that colon cancer may be associated with distinctive changes in intestinal bacteria. A study presented at the United European Gastroenterology Week (UEGW) in Stockholm, Sweden, and selected as one of the top five congress abstracts found that not only was the composition of bacteria in the stools of patients with colon cancer significantly different to healthy individuals, but that when these bacteria were transferred into the colons of healthy mice, pre-cancerous lesions developed.¹ Professor Iradj Sobhani from the Henri Mondor Hospital and University Paris-Est Créteil in France told journalists at the UEGW meeting that the results of this study can potentially open the possibility of mass screening for colon cancer. “Our studies provide clear evidence that carcinogenic factors are present in the stools of colon cancer patients and point to abnormal intestinal bacteria as the key suspect,” he said.

Bacteria and the colon

The human colon contains billions of bacteria – called microbiota – that form a well-organised, largely beneficial society. One of the main functions of microbiota is the modulation of immunity and protection against pathogens and diseases. There is, however, growing evidence that changes in bacterial populations or the products of bacterial metabolism may contribute to disease, with some initial studies suggesting an association between microbial imbalances (dysbiosis) and the risk of colon cancer.

“Until relatively recently, the only way to identify and analyse bacteria was to use specimen cultures, which are far from ideal, as around 60% of bacterial species won’t grow in culture dishes or milieu,” explained Prof. Sobhani. “Whole genome sequencing has now made it possible to characterise the biodiversity of microbiota, which has helped us to study bacteria in the intestines of normal and diseased individuals.”

Dysbiosis and colon cancer

Prof. Sobhani and co-workers have undertaken groundbreaking research on the association between intestinal bacteria and colon cancer. In their first study,² stool samples from a large number of individuals undergoing colonoscopy were analysed for bacterial DNA. Around one-third of the individuals were found to have colorectal cancer, while the rest were normal.

A comparison between the bacteria found in the stools of colorectal cancer patients and the normal individuals identified significant differences, with a marked elevation in the *Bacteroides/Prevotella* populations that appeared to be associated with an increase in infiltrating immune cells (IL17 cells) in the tumour samples.

“This study produced convincing evidence that the composition of bacteria in the stools of patients with cancer is markedly different to normal individuals,” said Prof. Sobhani. “This offers the intriguing possibility of using microbiota as a sensitive marker of colon cancer in the future.”

In a second study described by him, fresh stool samples were collected from individuals with colon cancer and healthy individuals and transferred to the colons of healthy germ-free mice by gavages, and the animals were followed up to 6 weeks.¹ The composition of bacteria in mice’s stools was of human type and remained stable over time. However, cell proliferation – an early cancer marker – and aberrant crypt foci (ACF) – an equivalent in mice to adenomatous polyps in humans – increased in the colons of mice given the cancerous stools. “This is the first evidence that the bacteria from the intestines of colon cancer patients are carcinogenic in germ-free mice,” said Prof. Sobhani. “We now need to try and identify which groups of bacteria are involved in the development of colon cancer so we can go on to improve mass screening programmes in healthy individuals and to assess response to chemotherapy and, ultimately, prognosis in those patients suffering from colon cancer.”

References

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2. Sobhani I, Tap J, Roudot-Thoraval F, et al. Microbial dysbiosis in colorectal cancer (CRC) patients. PLoS One. 2011 Jan 27; 6(1): e16393.

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