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INDEX 2009

From 4 to 6 October 2009, a further world conference of the STS (Science and Technology in Society) forum took place in Kyoto, Japan. The Kyoto Conference had acquired in our country already earlier a mark assigned to it by the media of a mere green action against environmental pollution. Its scope is, however, much wider. With some exaggeration we can say that it is focused against the "pollution" and ballast clogging of a variety of human endeavour fields, especially those of existence. It primarily searches for scientific tools and intellectual alliance to face current risks, whether on a global, supranational, or supraregional scale. It is a gathering of the leading physicists, power engineers, environmentalists, biologists, doctors, science organisers, businessmen, representatives of academic circles as well as of large industrial corporations.

The Kyoto Conference is concerned with the main contemporary issues of human society which, apart from environmental protection, sustainable development, new trends in power engineering development, and effective collaboration of non-profit and commercial sectors, also include the less medialised problems of reasonable and available health care and especially education. Education, awareness of the population, knowledge-based society, and the role of scientists in educational processes formed the centrepiece of all specialised topics at the STS forum conference. It is namely becoming apparent that the partial technological successes and a certain advance in the social hierarchy of contemporary populations are paradoxically accompanied by an education deficit, even despite the overwhelming flood of information, which is a sign of the times.

The difficult path from information to real knowledge and comprehension of priorities, and from these to wise acting has been designated as being a responsibility of the scientific elite. We have namely, even in countries with sufficient resources, been constantly confronted with unwise, ineffective, and unsustainable acting. Many examples were heard concerning this topic. The elaboration of the "information - knowledge - wisdom" line is an urgent task of not only scientific but also entrepreneurial and political elites.

Particular attention was given to the relationship between research and education. The conference completely refused the isolation of the scientific elite from education, an a priori emphasis laid on merely applied research and commercial supervision of science. At the academic level, the scientist has also to teach, the teacher has to be scientifically competent, the research has to be guided by goals higher than just immediately commercial ones.

For the citizen of the Czech Republic it is naturally disturbing that the attitudes of significant personalities at the conference, including several Nobel Prize winners, are oftentimes opposite to the contemporary trends set in our country in the interest of commercial control of research, which, however, imply a reduction of free science and education. What is also problematic is the Czech attitude concerning separation of the top-level science and educational experts, which is manifested in a sort of permanent competition between institutes of the Academy of Sciences of the Czech Republic and Czech universities for prestige, performance, and resources. This is considered at least as unwise waste of energy and the real potential of scientific education teams.

A variety of inspiring suggestions on methods of education and popularisation of scientific knowledge in the public in establishing a wider scope of erudition in society have sounded at the conference. Especially engaging was the address delivered by Professor Richard Ernst, winner of the Nobel Prize for his discovery of high resolution nuclear magnetic resonance spectroscopy, who with brilliant conciseness and aptness articulated the basic problems of the relationship between science and education as well as the role of academics. Here we bring it to the readers of Scripta Medica with the author's personal consent in the original English version.

Prof. MUDr. Jan Žaloudík, CSc.
The Dean of the Faculty of Medicine
Masaryk University

(Translated by L. Červený)

Lights and Shadows of Science and Technology in Today's Society

Richard R. Ernst, ETH Zürich, Switzerland

I was asked to add a few grains of pepper to the dinner menu by some remarks on the *Lights and Shadows of Science and Technology in Today's Society.* – Science and technology are neither bright nor dark, neither good nor evil. They function merely as tools; and tools are neutral, capable to all kinds of use and misuse.

Obviously, to discuss lights and shadows, we must address the goals and intents for which the tools are used. In my opinion, there is just one relevant goal, namely to serve today's as well as tomorrow's society by all available means. Winning prizes, becoming famous, becoming rich, and having a good life as our bankers in spacious land houses are no respectable goals for science and technology; in contrary, they might even be indicative for excessive selfishness and misuse of societal resources. Fortunately, the infamous bonus disease did not yet infect science.

Being researchers, we should not ask primarily for freedom of research. Instead, we should prove by the choice of relevant problems our willingness for behaving responsibly towards society. When we serve those who need moral, scientific, or technological support, a feeling of personal liberty and freedom of mind will follow spontaneously. John D. Rockefeller, Jr. once said: *"I believe that every right implies a responsibility; every opportunity, an obligation; and every possession, a duty."*

Please remember that research is first of all a means of education, a means of acquiring knowledge. Research is by far the best way of "learning by doing", the best way of experiencing nature by posing incisive questions and answering them by experiments. A well equipped laboratory is infinitely more useful for efficient learning than a fancy lecturing hall. We should never separate research and education! Stand-alone research institutes without educational obligations are for me a luxurious waste of resources.

Research can be driven by pure curiosity; but more often, it is from the beginning application-oriented, with a clear goal in mind, trying to satisfy a public need. And as a side-effect, it might even be serving industry. - To use my personal example, I never considered myself being a true scientist but rather an engineer, who made Nuclear Magnetic Resonance to work in a wide variety of exceedingly useful applications. Usefulness was my goal from the beginning and to the very end of my career as a researcher. – NMR and MRI succeeded without much sales promotion; their utility was so plainly obvious. We all know, sales promotion is indispensable merely for selling unnecessary products that better would never had been produced at all. In fact, the promotion of useless gadgets complicates our daily life without any benefit, degrading us to slaves of technology. Examples are plentiful; just watch our children's hypes!

Instead of sales promotion, society urgently needs continuing education by providing reliable information, receiving advises for reducing consumption, preserving resources for future generations, and saving our precious time for a life rich in content instead of becoming rich in distraction and idling nonsense. Public teaching is indeed a most important obligation of academic institutions for opening public eyes towards potential future catastrophes, such as global warming, plundering of resources, and overpopulation.

How can we teach responsible behavior to the public as long as fraud is still a recurring fact at our universities? The excuse that even researchers are human beings does not help in this situation. Honesty in research and education is more important than all the conveyed specialized knowledge. Much more emphasis than in the past should to be put on aspects of honesty and responsibility in university education.

But as long as scientists are driven by competition, by alluring prizes, by the request of long list of publications, and by insane university ranking agencies, no hope is insight. In fact, the academic situation is just a reflection of the prevalent capitalistic free market business model that has last year failed to all extent and lead to a catastrophe on the financial market that required remedies by the otherwise ridiculed Nation States. Personal gain and egoism dominate today our short-sighted business model, following the well-known and, in fact, utterly immoral quotes by Adam Smith. The "invisible hand" and the stabilizing negative feedback loop of free market economy, unfortunately, are inoperative on a global scale and for longer time spans. – Instead of copying within our academic institutions and think-tanks this irresponsible behavior, it would be more urgent to develop new business models

and models of behavior based on foresight, ethical principles, and sustainability that lead to what I often call a "responsible market economy" instead of a "free market economy".

Certainly, without science and technology, mankind has no future; but with science and technology alone, we will shuffle our own grave for ending prematurely a senseless life as robotic operators. For replenishing our life with meaning and with sense, we need, in addition, very personal passions outside of science and technology; we need a "second leg". We need *wisdom* for comprehending the dangers lurking along the future pathway, and *compassion* for relating to our, possibly needy, compatriots and for establishing long-lasting human relations.

Remember, science and technology are just tools, as mentioned at the beginning. Their proper usage requires foresight and responsibility, in the sense of the philosopher Hans Jonas who formulated the "Imperative Responsibility": *"Act so that the consequences of your actions are compatible with the permanence of genuine human life on Earth."* Clearly, his saying boils down to ultimate sustainability. Indeed, sustainability forces us to assume responsibility for the fate of our descendents. Let us act invariably as if a sorrowful solicitor of future generations would look over our left shoulder! For example, when we consume too much meat or when we are driving our fuel-wasting SUVs.

And for those of you who feel great from time to time, and I hope all of you do, Winston Churchill once remarked: *"Responsibility is the price of greatness."*

Thank you for your kind attention to my Sunday evening sermon!

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Ladies and gentlemen,

The scientific journal of the Faculty of Medicine of Masaryk University, Scripta Medica, has been published since 1922. In these more than 80 years, tens of gastroenterological papers have been published. Nevertheless, this issue of Scripta Medica is the first in the history to be completely dedicated to gastroenterology and hepatology. It is my great pleasure to present 12 papers, coming mostly from my young colleagues not only from our Department of Internal Medicine and Hepatogastroenterology of the Faculty of Medicine of Masaryk University but also from the well-known gastroenterological or hepatological centres in Hradec Králové, Ostrava, and Frýdek-Místek.

Gastroenterology and hepatology are parts of medicine which have seen tremendous expansion during the last years. The progress in diagnostic procedures and therapeutical possibilities is enormous. I hope that we will be able to present at least part of this progress in this issue of Scripta Medica.

In the first paper, Klímová reports on some new methods of investigation of the small bowel, an organ which had been very hard to investigate a few years ago. Balloon enteroscopy and capsule endoscopy are procedures that are of great benefit in the imaging of the small intestine. Stibůrek et al. described a brand new use of capsule endoscopy in the investigation of the large intestine. In spite of enthusiasm in this field, the first results are not too optimistic, but technical progress can diminish current difficulties in the future. It seems that some benefit in the investigation of the colon could be reached by improving standard colonoscopy. Kliment et al. described improved visualisation of the colorectal mucosa and increased adenoma detection using high-definition, high-resolution, wide-angle colonoscopy. Electrogastrography is an appealing investigation of the stomach. Prokešová et al. described this completely non-invasive measurement of gastric myoelectrical activity, unfortunately with limited clinical impact. However, even old methods could be effectively used in new indication. Kajzrlíková et al. presents the usefulness of abdominal ultrasound for the detection of hepaticojejunoanastomosis-related complications.

Ševčíková et al. reports on a relevant case of acute pancreatitis with a short history complicated by invasive ductal pancreatic adenoma – an infrequent but serious issue. Two papers give an account of hepatology. Trumpešová et al. describes a not very frequent but important liver disease – primary sclerosing cholangitis. Hůlková et al. found some very interesting psychiatric aspects of liver encephalopathy. Intestinal microflora and bacterial translocation seem to play a crucial role not only in the above-mentioned liver encephalopathy but also in many other gastroenterological diseases. Lata et al. describes this broad issue.

Šlapák et al. defines a growing problem – obstipation and diarrhoea in the elderly population. Even general practitioners have been facing this problem due to the increasing number of seniors in the population. Mišejková et al. describes the important general problem of therapy – adherence to treatment. Limited knowledge or misinformation was the main reason for non-adherence in a group of patients with inflammatory bowel disease. Fojtík et al. focused their paper on a very frequent but underdiagnosed illness – coeliac disease. It is diagnosed very rarely, especially in older age, but it is clear that osteoporosis could be a very important symptom.

The year 2009 has started a new epoch of the journal Scripta Medica. I am glad that we have had the opportunity to publish our papers in this year's last issue of Scripta Medica.

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INTERNÍ
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NEW METHODS OF SMALL BOWEL INVESTIGATION

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KEY WORDS

Capsule endoscopy
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ABSTRACT

The anatomy of the gastrointestinal tract can be investigated by both invasive and non-invasive methods. Most frequently endoscopy or double-contrast radiological techniques are used. The part of the small intestine between the duodenum and terminal ileum is difficult to reach by standard endoscopy. However, it can be judged by radiological enteroclysis, which has the disadvantage of exposing the patients to X-rays; moreover, it is impossible to examine the pathological findings histologically. New and more accurate enteroscopic (single- and double-balloon including intraoperative) methods and capsule enteroscopy have been coming into wider use.

Capsule endoscopy is an endoscopic method that enables to examine the whole small intestine. This technology consists of swallowing a capsule in size of a large vitamin tablet, which is later moved forward by the motility of the gastrointestinal tract distally. The record is then evaluated by a doctor.

Intraoperative enteroscopy is still more often substituted by balloon enteroscopy. However, it remains an option when the classical double-balloon enteroscopy did not solve the patient's problems definitely, that is mainly in patients with intestinal adhesions or multiple lesions of small intestine.

Balloon enteroscopy is a modern method that is used to examine the whole small intestine, which also enables us to carry out therapeutic efforts when the routine endoscopy was not successful. In some indications it has substituted intraoperative enteroscopy.

These three methods are complementary and cannot be replaced by each other. Some authors consider them as the golden standard in the investigation of small intestine.

INTRODUCTION

Small intestine is the longest part of the gastrointestinal tract starting in the duodenum and ending in the ileocaecal region. The length of the small intestine varies significantly during life (from 200 cm in the newborn up to 300 to 600 cm

in the adult). Anatomically it can be divided into three parts: duodenum, jejunum, and ileum. The duodenum is approximately 30 cm long, the jejunum represents almost one half of the total length of the small intestine. Its mucosa is enlarged by transverse folds and mainly by the presence of minute fingerlike projections known as villi and microvilli. The wall consists of mucosa, submucosa, smooth muscle, and serosa. The mucosa is lined with simple columnar epithelium with brush borders (microvilli). Among the villi there are tubular glands (Lieberkühn glands – glandulae intestinales). Among the enterocytes there are goblet cells which are specialised for the secretion of mucus.

The most frequent pathological findings include functional changes, inflammatory bowel disease (Crohn's disease, ulcerative colitis), specific and non-specific enteritis, tumours, obstructions, ischaemias, or malabsorptions. Currently there are different methods that can be used in order to reach fast and correct diagnosis.

RADIOLOGY

Various radiological methods are used to investigate the small bowel. Of the conventional methods the most important are enteroclysis and ultrasound of the bowels. The main disadvantage of these methods is that they strongly depend on the experience of the doctor who evaluates them. Angiography is used in order to look for abnormalities in the blood vessels; it can also be used to treat acute intestinal bleeding.

BLEED SCAN

Methods offered by nuclear medicine are not frequently used in gastroenterology. There are two main indications for these investigations: firstly bleeding into the gastrointestinal tract – here it can answer two main questions – the location of the bleeding and the volume of the blood loss, and secondly tumours [1].

ENDOSCOPY

Endoscopic procedures are irreplaceable as far as early diagnosis is concerned. In an endoscopic procedure, the physician inserts a thin, lighted, camera-tipped tube (endoscope) either through the mouth or rectum inside the body. The patient is sedated before the procedure.

During a standard gastroscopy it is usually possible to investigate the proximal part of the duodenum (D1–D3) [2]. Push-enteroscopy is of an excellent diagnostic value as far as the duodenum and the proximal jejunum (94 %) are concerned; however, its main disadvantage is the limited reach that dramatically decreases its overall value for investigating lesions in the small bowel (53 %) [3]. This method is still used in places where the double-balloon technique is not available. The enteroscopes are actively inserted by the endoscopist. Usually it is possible to reach 60–130 cm behind the Treitz ligament at maximum. Compared to the balloon enteroscope it is more difficult to control the push-enteroscope and the value of the investigation is not so high [4]. During the routine colonoscopy we can insert the endoscope retrogradely into the ileum and investigate approximately 30 cm of the terminal ileum.

The fundamental advantage of endoscopic methods is the possibility of judging the investigated region of the small intestine visually. Moreover, we can take biopsies or perform therapeutic procedures (polypectomy, APC – argon plasma coagulation or mucosectomy). The value of the optical evaluation can be increased by filtrating the wave lengths of the white light in a new method called Narrow Band Imaging (NBI), which can distinguish between premalignant and malignant lesions. With the contribution of NBI mucosal lesions can also be judged by zooming the endoscope onto the mucosa with conserved sharpness of the image [5]. In local differential diagnostics, chromodiagnostics can also be used. To demonstrate superficial mucosal lesions absorptive dyes (methylene blue) or contrast dyeing (indigocarmine) are used. Most often they are applied through spray catheters to visualise a particular lesion or the mucosa of the whole intestine (panchromoendoscopy) [6]. Chromodiagnostics with zooming onto suspicious lesions have enabled the creation of a so-called pit-pattern classification according to Kudo. The findings on the intestinal mucosa are divided into 5 types. "Pit pattern" 1–2 predicts non-tumorous lesions and "pit pattern" 3–5 corresponds with intraepithelial neoplasias (dysplasias or invasive carcinoma) [6]. Another option is represented by "endoscopic microscopy". This includes the confocal microscopy, i.e., non-invasive optical imaging of the mucosa with laser scan of a certain wavelength. It allows us to analyse the mucosa into a depth of 200–500 nm with the reflected light. Another very promising technique is represented by endocytoscopy, in which we can magnify the mucosa 1200–fold using standard endoscopy. In combination with chromoendoscopy you can get a very accurate and detailed picture of the mucosa right during the investigation or you can modify next steps [5].

Nowadays new techniques such as enteroscopy and capsule endoscopy have been coming into wider use. These three methods complement each other and follow each other in the investigation algorithm; they cannot be replaced by each other. Some authors consider them as the golden standard for investigation of the small intestine.

CAPSULE ENDOSCOPY

Capsule endoscopy represents a new diagnostic procedure that was introduced into clinical practice in 2001 and since then its use has developed significantly. It is a highly

specialised minimally invasive endoscopic method designed to investigate the small bowel, oesophagus or colon, which has over the last few years become an important part of the diagnostic algorithm of the examination of the small bowel. In the Czech Republic it has become relatively easy to reach and perform. The diagnostic system includes an endoscopic capsule, a system of antennas, a data recorder, an analyser, and a working station. The endoscopic capsule that the patient swallows enables us to scan the endoscopic picture during its passage through the gastrointestinal tract and its wireless transfer [7].

Not only can we investigate the whole small intestine, but also the oesophagus or the colon; however, in these locations it cannot compete with endoscopy. For the patient this method is more than acceptable – they swallow a capsule in the size of a large vitamin tablet, which includes a miniature colour video camera, a light, a battery, and a transmitter. The capsule is later moved distally by the motility of the gastrointestinal tract. It is therefore completely dependent on the quality of the motility of the gastrointestinal tract (it can stay in the stomach for a long time). There is a risk of "saltatory" moving due to increased gut motility together with a change in the patient's position – thus significant pathologies can be missed. Also, we cannot forget the risk of possible transitional covering of the capsule by the content of the bowel or stagnation due to a stricture (which is also a contraindication of this procedure). The price of this method (the capsule itself is worth approximately CZK 15 000) is also fairly high.

Important complications are rare.

The main disadvantages of this tool are that the camera cannot be controlled and lesions cannot be treated or biopsies taken at the time that they are discovered.

In our country capsule endoscopy is used only for investigation of the small intestine on the routine basis. It serves as an additional diagnostic procedure for patients who suffer from unexplained gastrointestinal disorders, such as bleeding, or to evaluate conditions of the small bowel that cause diarrhoea, pain or weight loss, such as Crohn's disease [10].

INTRAOPERATIVE ENTEROSCOPY

Intraoperative enteroscopy is an endoscopic method that enables the investigation of the whole small intestine, allowing to perform diagnostic (biopsies of mucosa) or therapeutic procedures (electrocoagulation, polypectomy) at one time. Endoscopically unsolvable pathological findings can be solved by the surgeon within seconds – during the same anaesthesia. Its disadvantage is its invasiveness, the necessity of anaesthesia, and laparotomy (laparoscopy) (8, 9).

It was the first enteroscopic technique brought into practice before balloon enteroscopies. Its main advantage is the possibility of viewing incomparably bigger parts of the small intestine than was allowed by the technique of enteroscopy used until then, introduced maximally with the support of an overtube. Co-operation with the surgeon made it much easier to move the endoscope in the intestinal lumen, to view the anatomical variations of the small intestine in high detail and, in the case of a positive finding, to immediately perform the necessary operative intervention. The disadvantage was the necessity of anaesthesia. Currently, this procedure is being substituted by balloon endoscopy. However, it remains an option when the classical double-balloon enteroscopy did not solve the patient's problems definitely, that is mainly in patients with intestinal adhesions or multiple lesions of the small intestine.

BALLOON ENTEROSCOPY

Single- or double-balloon enteroscopy is another modern endoscopic method that allows the investigation of a bigger part or even of the whole small intestine. The investigation of the whole small bowel is rarely possible from the oral access; more often it is a combination of oral and aboral access, i.e. a combination of two investigations [8].

It enables us to carry out therapeutic procedures in situations when the routine endoscopy has failed. In some indications it has replaced the intraoperation enteroscopy, which remains an irreplaceable method when DBE cannot investigate the whole small intestine [11].

Currently there are two systems available: double-balloon – using a system of two balloons insufflated externally. One of them is placed on the overtube and the other is firmly connected with the end of the enteroscope. By alternate insufflation and desufflation of the balloons while moving the enteroscope with the overtube the whole system is pushed inside the lumen of the small bowel distally – ideally as far as the Bauhin's valvula. In case that it is not possible to reach the appropriate position perorally, then the position that had been successfully reached is marked with a special dye and the rest of the bowel is then examined transrectally.

The position of the balloon in the end of the enteroscope does not allow its protrusion during the procedure.

Single-balloon technology is very similar. The only difference is that at the end of the enteroscope there is no balloon, so the contact between the system and the bowel is kept by the pressure of the endoscope on the intestinal wall.

Lately, new modifications have appeared on the market: [1] putting the insufflation balloon directly on the outer surface of the endoscope and inserting the other balloon through the bioptic canal of the enteroscope; [2] a helix placed externally on the enteroscope, which moves the enteroscope distally by its rotation. Both of these systems have been available only for a short time and need to be verified by longer clinical experience.

CONCLUSION

In the past decade, our hospitals and medical centres have been flooded by a great number of new, direct and indirect diagnostic methods. Some of them have become an important part of the routine examination – enteroscopy is the most obvious example of this fact. The development is fast due to the fast development of the technical abilities of video endoscopes and computer technology. The new methods, such as capsule endoscopy, intraoperative enteroscopy and double-balloon enteroscopy, represent a group of complementary investigations, whose value needs to be verified by longer studies. However, they are already considered by some authors as the golden standard in the diagnosis of small bowel abnormalities.

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CAPSULE COLONOSCOPY

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INTRODUCTION

Capsule endoscopy (CE) has already become an integral part of the diagnostic algorithm for small bowel diseases [1]. This method is now quite easily available in the Czech Republic and is performed in more than 20 centres. A new method – capsule colonoscopy – has been available since the beginning of 2008. In this paper we present our experience with this method.

TERMINOLOGY

Based on the type of the capsule, CE is a method designed for the examination of small bowel, large bowel, or oesophagus. The examined patient swallows the capsule and its passage through the gastrointestinal tract (GI) enables wireless transmission of the endoscopic image.
The diagnostic system includes an endoscopic capsule, a sensor system, a data recorder, a real time viewer, and a workstation. In the present days there are similar systems produced by two companies: "Given" and "Olympus" (the Olympus system is designed for small bowel examination only).
Technically, an endoscopic capsule consists of a digital camera located in a plastic capsule which is 26 mm long and 11 mm in diameter (31 x 11 mm is the colonic one). The capsule is passively passed through the GI tract during the examination by peristalsis and records 2 pictures per second (the oesophageal capsule records 14 pictures per second). The data is immediately sent to the sensors (the antenna array) placed on the patient's body and then to the data recorder. The capsule records image data for 8–12 hours, as long as allowed by the batteries' lifespan.
Realtime Viewer is a portable computer-like device with special software enabling us to watch the real-time endoscopic image. This is important for localising the position of the capsule within the GI tract. We should use it after 2 hours since the capsule has been swallowed and when the capsule remains in the stomach, it should be removed to the duodenum by the gastroscope.

The workstation is represented by PC with a dock station for the data recorder and the software for data downloading and endoscopic image browsing.
The examination of the small bowel takes 8 to 10 hours; the capsule usually leaves the body per vias naturales after 1 to 7 days. Preparation for this examination is quite simple: deflatulents and fasting with increased fluid intake during the day before the examination [2].
The capsule endoscopy of the small intestine is a highly specialised and relatively expensive method. Therefore, in the Czech Republic it remains as the last diagnostic option in case that other endoscopic methods fail to reveal the diagnosis.

CAPSULE COLONOSCOPY

Since the beginning of 2008 the use of capsule colonoscopy has been approved for commercial use in the Czech Republic. There are some differences between the more common small intestine capsule and the colonic capsule. The colonic one has two cameras, one at each end of the capsule, and is 5 mm longer (with the same diameter). It takes 4 pictures per second – 2 pictures for each camera. The optical system is improved and optimalised. Three minutes after being swallowed the capsule switches to the sleep mode for 105 minutes to save the battery. By the time it turns on again, it should be somewhere in the small intestine. The bowel preparation for the examination is very important and the colon has to be as clean as possible. For the cleaning of the colon and the right course of the examination we use in total 6 litres of electrolyte lavage solution (4 litres before and another 2 litres during the examination) and prokinetics (domperidone is used in our practice) (3,4,5). The capsule has to leave the human body no later than after 11 hours, so a suppository or a retrograde enema could be useful at the end.

Based on the next six short case reports, we would like to express our recommendations and comments for capsule colonoscopy.

Case 1
A male, 47 years old, with dyspepsia, occasional diarrhoea, colonoscopy was recommended. He explicitly refused all classic endoscopic methods. After the first 5 hours and 30 minutes the capsule was still retained in the stomach, but he refused gastroscopic relocation into the duodenum. The examination ended incompletely after 11 hours. The recording ended in the colon descendens. A small polyp (about 3mm) was found in the colon ascendens, and the patient was at least persuaded into endoscopic polypectomia.

Case 2
A female, 63 years old, with dyspepsia and mild obstipation, type 2 diabetes mellitus, colonoscopy was recommended and refused by her. The bowel prep was poorly tolerated and the patient finally insisted on termination of the examination after 8 hours and 30 minutes. The examination was therefore incomplete and ended in the descending colon. Diabetic impairment of GI transit could play a role, but the examination was terminated two and a half hours longer.

Case 3
A female, 37 years old, with ulcerative colitis. She had a history of very poor toleration of classic coloscopy and therefore had not been examined for more than six years. She tolerated the bowel prep very badly and the examination was incomplete after 11 hours, which is very unfortunate especially in an ulcerative colitis patient. She suffered a cramp attack several hours after the examination, caused by the ion imbalance because of the large (yet standard) amount of the lavage solution.

Case 4
A male, 40 years old, obese, with a family history of colorectal carcinoma. He demanded capsule colonoscopy, although the classic one was recommended. After 105 minutes, the capsule started to record already within the colon. There were no records of the caecum. The remaining parts of the colon were without pathology.

Case 5
A female, 53 years old, with dyspepsia, to whom colonoscopy was recommended. She underwent several abdominal surgeries and thus had a history of very painful classic colonoscopy. She even refused the procedure under deep analgosedation. Diverticula and at least 5 polyps were revealed by capsule colonoscopy. After this she underwent coloscopic removal of the polyps in deep analgosedation.

Case 6
A male, 51 years old, with a positive occult bleeding test. He did not follow the guidelines and drank only 3 litres of electrolyte lavage solution before the examination and another 2 litres during the examination, because he felt the preparation was adequate. Therefore we discovered large amounts of faeces, which disabled the examination.

Indications for capsule colonoscopy

The cases where classic colonoscopy could not be performed (e.g. adhesions after previous abdominal or pelvic operations) should be the main indication. It can also be used in patients who strictly refuse classic colonoscopy.

ADVANTAGES

It is a non-invasive examination, without sedatives, intubation, insufflation, no radiation load is involved, and it is painless for the patient. The whole examination is performed by a nurse; the physician evaluates the records later and the record is always fully available.

DISADVANTAGES

The main disadvantage is the price of the examination. Health insurance companies in the Czech Republic do not cover capsule colonoscopy. The full price has to be paid by the patient (ca. CZK 17500). Non-invasiveness cannot always be considered an advantage. CE is not capable of bioptic sampling and/or therapeutic interventions. A successful CE examination is conditioned by excellent bowel preparation and thus every bowel content residuum decreases the diagnostic yield noticeably. Furthermore, CE is a passive process without the possibility of insufflation, rinsing, and draining. The capsule is not always excreted after 11 hours or is already in the colon after the 105 minutes when it switches on; thereby the examination is often incomplete from one or another side (orthogradely or retrogradely). In most cases classic colonoscopy has to be finally done with the pathological findings.

OUR RECOMMENDATIONS

1. The patient's case has to be undoubtedly indicated for colonoscopy.
2. Patients have to be thoroughly informed about all advantages and disadvantages of CE. The recommendation of classic colonoscopy with the possibility of deep analgosedation is the most important part of the protocol.
3. Using the Real Time Viewer is necessary at least once (after two hours since swallowing the capsule) during the examination to demonstrate current position of the capsule (all possible steps have to be taken for the right course of the examination).
4. Most of the patients who want capsule colonoscopy should be persuaded into the classic one because their requirements are associated with lack of information and not with the necessity for CE exam.
5. Strict preparation (colon cleaning) for the examination is essential and cannot be underestimated. Unfortunately, even full compliance of the patient with this intensive bowel cleaning protocol can be insufficient in some cases.
6. Monitoring of patients with IBD (especially with UC) by capsule colonoscopy seems unsuitable because of a relatively large risk of incomplete examination.

CONCLUSION

Capsule colonoscopy is a modern and sophisticated examination method with its specific indications, but it will probably not reach common use in everyday practice because of its limits and extra price.

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HIGH-DEFINITION, WIDE-ANGLE COLONOSCOPY FOR ADENOMA DETECTION – A PROSPECTIVE STUDY

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AFFIRMATION

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ABBREVIATIONS USED

HDWAC – high-definition, wide-angle colonoscopy
SRSAC – standard-resolution, standard-angle colonoscopy
HRSAC – high-resolution, standard-angle colonoscopy
CRC – colorectal cancer
CCD – charged couple device
HG IEN – high-grade intraepithelial neoplasia

ABSTRACT

Improved visualisation of colorectal mucosa may increase adenoma detection. The objective of our study was to compare high-definition (1080–line screen), high-resolution (≥400 000 pixels), wide-angle (170°) colonoscopy (HDWAC) with standard-resolution (≤300 000 pixels), standard-angle (140°) colonoscopy (SRSAC) and high-resolution, standard-angle colonoscopy (HRSAC), both combined with standard-definition (480–line) screen, in terms of adenoma detection. A total of 507 consecutive patients presenting with diagnostic colonoscopy were allocated to undergo either SRSAC (n=254), or HRSAC (n=160), or HDWAC (n=93). The primary outcome parameter was the difference in adenoma detection between the study groups. The mean number of adenoma and flat adenoma detected per patient was higher in HDWAC than in HRSAC and SRSAC groups (adenoma±SD: 0.91±1.27 vs 0.63±1.19 vs 0.59±1.15, respectively, P=0.014; flat adenoma: 0.45±0.81 vs 0.28±0.77 vs 0.15±0.51, respectively, P<0.001).

The proportion of patients with ≥1 adenoma of any size and ≥1 adenoma <10 mm with advanced histology (containing either high-grade intraepithelial neoplasia or villous morphology) was higher in HDWAC compared with SRSAC and HRSAC groups (any adenoma: 48.4 % vs 32.3 % vs 34.4 %, respectively, *P*=0.019; adenoma <10 mm with advanced histology: 16.1 % vs 7.1 % vs 5.0 %, respectively, *P*=0.005). HDWAC improves adenoma detection when sufficiently long instrument withdrawal time is kept. This is primarily accounted for by increase in the detection of adenomas, including flat adenomas and adenomas with advanced histology, <10mm in size. These findings support the use of HDWAC in clinical practice.

INTRODUCTION

The interruption of adenoma-carcinoma sequence is the primary end point of colorectal cancer (CRC) screening and colonoscopy is the best tool to achieve this goal. The first studies on incident CRC rates after clearing colonoscopy proved to prevent approximately 80 % of CRCs [1,2]. Later studies, however, demonstrated a substantially lower protective effect of colonoscopy [3–5], which may in part be explained by missing adenomas during colonoscopy [6,7]. The reasons for missing adenomas are either procedure- (incomplete colonoscopy, fast endoscope withdrawal, ineffective polypectomy) or instrument- (inability to expose mucosa on proximal sides of folds or to detect flat adenomas) related [8].

To expose more colorectal mucosa and to detect flat adenomas, several colonoscopic techniques, including wide-angle viewing colonoscopes [9,10], cap-fitted colonoscopy [11], colonoscopy in retroflexion [12], chromoendoscopy [13,14], narrow band imaging [15], and high-definition colonoscopy [16,17], have been studied with mixed results. The studies from Europe [18,19], and US [20] have shown similar prevalence of flat adenomas to that reported in Japan. The miss rate for flat adenomas may be significantly higher than for adenomas of sessile or pedunculated pattern [21]. Since this subgroup of adenomas may carry a higher risk for malignant transformation, especially of depressed type [22], they should not be missed but treated during colonoscopy, which offers efficient and safe therapy [23].

Conventional videoendoscopes, equipped with charged couple device (CCD) chips of 100 000 to 300 000 pixels, are referred to as standard-resolution endoscopes. Videoendoscopes equipped with CCD chips of ≥400 000 pixels are referred to as high-resolution. High-definition endoscopes produce a video signal with 1080 visible horizontal scan lines, whereas a video signal produced by standard-definition endoscopes consists of 480 lines. It is hypothesised that endoscopes with higher image resolution and wider angle view should detect more adenomas, including flat adenomas. But to date no study has confirmed this hypothesis. In our study, we sought to confirm whether high-definition, wide-angle colonoscopy (HDWAC) detects a higher number of adenomas and flat adenomas compared with standard-resolution, standard-angle colonoscopy (SRSAC), and high-resolution, standard-angle colonoscopy (HRSAC).

MATERIALS AND METHODS

Patients were eligible if they were aged ≥18 years and presented with diagnostic colonoscopy. The exclusion criteria were as follows: active gastrointestinal bleeding, inflammatory bowel disease, familial polyposis syndromes, hereditary non-polyposis colorectal cancer, inability to pass the endoscope beyond the sigmoid colon, and inability to give informed consent. The study protocol was approved by the Institutional Review Board and the Ethics Committee at Vítkovice Hospital. The patients were enrolled between November 1, 2006 and May 31, 2007.

Colonoscopies are performed in parallel in 2 suits in our endoscopy unit and the patients are scheduled in 45 minutes' intervals. Cleaning the instrument takes approximately 45 minutes. Depending on the availability of the endoscope, patients presenting with diagnostic colonoscopy were assigned to undergo either SRSAC or HRSAC or HDWAC. In the SRSAC group, three standard-resolution, standard-angle (140°) view videocolonoscopes (Olympus CF Q145, CF Q145L; Olympus Europe, Hamburg, Germany) with a standard-definition 480–line screen were available. In the HRSAC group, colonoscopies were performed with one of the two high-resolution, standard-angle (140°) view videocolonoscopes (Pentax EC 3881 FK, EC–3870 FZK; Pentax Europe, Hamburg, Germany) with a standard-definition 480–line screen. In the HDWAC group, a single high-resolution, wide-angle (170°) view videocolonoscope (Olympus CF HI 180 AL; Olympus Europe, Hamburg, Germany) with a high-definition 1080–line screen was available. Eight endoscopists with previous experience of ≥200 to ≥7000 colonoscopies participated in the study, conducted at a single non-university tertiary referral centre. All patients underwent bowel preparation consisting of solid food restriction and drinking either 4L of macrogol or 500mL of magnesium sulphate solution 24 hours prior to colonoscopy. The quality of bowel preparation was graded by the endoscopist as follows: [1] excellent – no solid or liquid residue, [2] good – complete mucosal inspection after suction, [3] fair – greater than 90 % mucosal visualisation, [4] poor – less than 90 % mucosal visualisation. After caecal intubation the withdrawal time measurement began and was stopped when the endoscope was withdrawn from the anus. The watch was stopped

Table 1
Demographics, colonoscopy baseline characteristics

Parameters	SRSAC (n=254)	HRSAC (n=160)	HDWAC (n=93)	*P* value
Patient demographics				
Mean (SD) age (years)	58.8 (14.9)	58.0 (15.6)	60.3 (11.6)	0.76
Male gender, N (%)	126 (49.6)	81 (50.6)	51 (54.8)	0.69
Successful caecal intubation, N (%)	244 (96.1)	156 (97.5)	90 (96.8)	0.73
Mean (SD) withdrawal time (min)	8.8 (1.8)	8.6 (1.4)	8.6 (1.5)	0.89
Indications				
Bleeding, N (%)	97 (38.2)	55 (34.4)	34 (36.5)	0.84
Change in bowel habits, N (%)	47 (18.5)	37 (23.1)	15 (16.1)	
Surveillance, N (%)	41 (16.2)	33 (20.6)	20 (21.5)	
Abdominal pain, N (%)	32 (12.6)	16 (10.0)	12 (12.9)	
Weight loss, N (%)	8 (3.1)	5 (3.1)	4 (4.3)	
Others, N (%)	29 (11.4)	14 (8.8)	2 (8.7)	
Bowel preparation				
Excellent : Good : Fair : Poor	116:76:32:30	84:35:18:23	39:29:14:11	0.46

Table 2
Detection rates of polyps and adenomas – per patient analysis

Parameter (±SD)	SRSAC (n=254)	HRSAC (n=160)	HDWAC (n=93)	*P* value
Polyps	1.06 (1.62)	1.15 (1.61)	1.48 (1.69)	0.008
Adenomas	0.59 (1.15)	0.63 (1.19)	0.91 (1.27)	0.02
Flat adenomas	0.15 (0.51)	0.28 (0.77)	0.45 (0.81)	<0.001
Polypoid adenomas	0.44 (0.97)	0.36 (0.79)	0.44 (0.84)	0.76
Right-sided adenomas	0.27 (0.65)	0.32 (0.77)	0.52 (0.99)	0.04
Left-sided adenomas	0.32 (0.70)	0.30 (0.64)	0.39 (0.71)	0.29

for polyp biopsy, polypectomy, and polyp retrieval. According to the international recommendation [24] an attempt was made to keep the extubation time at least 6 minutes in each study group. The morphology and size of each colorectal lesion were recorded. According to the Paris Endoscopic Classification of Superficial Neoplastic Lesions [25] the lesion was endoscopically classified as flat when it did not pass above the closed cups of a biopsy forceps (2.5 mm) (Olympus) placed adjacent to the lesion, whereas lesions passing above were classified as polypoid. The size was measured by placing a fully opened biopsy forceps next to the lesion. All detected lesions were removed by one of several resection techniques except for small lesions in the rectosigmoid which appeared to be hyperplastic, because their pit pattern was determined to be type I or II. The histology of all resected specimens was interpreted by two experienced pathologists using the Vienna Classification [26].

The primary outcome measure was the difference in adenoma detection between the study groups. The secondary measures were differences in flat adenoma, adenoma <10mm with advanced histology, defined as either high-grade intraepithelial neoplasia (HG IEN) or villous morphology, right-sided (caecum to splenic flexure), left-sided (splenic flexure to rectum), and multiple adenoma detection between the groups.

Statistical analysis

We calculated the sample size required to detect a significant improvement of adenoma detection with HDWAC compared

with SRSAC using the DSTPLAN software (http://linkage.rockefeller.edu/soft). Assuming a 20% prevalence of adenomas in the population, at least 250 patients undergoing SRSAC and 90 patients undergoing HDWAC were required for detection of at least 20% difference in the proportion of patients with adenomas. The calculations were performed at 5% of significance for 80% statistical power. One-way ANOVA, Mann-Whitney or Kruskal-Wallis tests, when appropriate, were used for comparison of continuous variables, and the Fisher exact test was used for comparison of proportions. To assess the role of clinical variables independently influencing the number of diagnosed polyps, stepwise linear regression analysis was used. Goodness-of-fit and co-linearity statistics were assessed for the regression model. The level of significance was set at $P<0.05$, P values between 0.05 and 0.10 were considered to indicate a statistical trend. All P values were two-sided. Statistical analysis was performed using SPSS version 14.0 (SPSS Inc., Chicago, IL).

RESULTS

A total of 524 consecutive patients referred for diagnostic colonoscopy fulfilled the inclusion criteria and were enrolled in the study. After exclusion of 17 patients because of either diagnosing IBD or the presence of non-transferable stenosis of rectosigmoid colon, 507 patients (50.9% male) with a mean age of 58.9±14.3 years completed the study protocol. A total of 254 patients were analysed in the SRSAC arm, 160 in the HRSAC, and 93 in the HDWAC arm. Table 1 shows that there was no difference between the study groups in any of the parameters assessed. No complication occurred in any patient included in the study. A total of 592 lesions with a mean size of 6.15±6.43mm (range 1.0–60.0mm) were detected in the entire study population, of which 255 (43.1%) were hyperplastic polyps, 305 (51.5%) adenomas with low-grade intraepithelial neoplasia, 26 (4.4%) adenomas with HG IEN, 3 (0.5%) intramucosal, and 3 (0.5%) invasive carcinomas. From the total of 331 adenomas, 206 (62.2%) were polypoid and 125 (37.8%) were flat according to the Paris Endoscopic Classification [25]. From the entire study group, at least one adenoma, one flat adenoma, and multiple (≥3) adenomas were detected in 182 (35.9 %), 80 (15.8 %), and 35 (6.9%) patients, respectively.

Table 2 demonstrates the summary of lesions found in per-patient analysis. The mean rate of adenoma and flat adenoma per patient was significantly higher in HDWAC group compared with the other groups (P=0.02, P<0.001, respectively). The mean number of right-sided adenoma per patient in HDWAC group was almost double that of SRSAC group (P=0.01). In contradiction to right-sided and flat adenomas, there was no difference in the detection of left-sided and polypoid adenomas between the study groups (P=0.29, P=0.76, respectively). The prevalence rates of adenomas and flat adenomas of various size, the prevalence rates of polypoid, right-sided, left-sided adenomas, and adenomas with advanced histology <10 mm in size are shown in Table 3. A subgroup analysis of the prevalence of adenomas <10mm showed a statistical trend towards a greater prevalence in the HDWAC group (P=0.07). When this subgroup was restricted to flat adenomas, there was a significantly higher prevalence of flat adenomas <10mm in HDWAC group (P<0.001). The proportion of patients with ≥1 adenoma <10mm in size with advanced histology was higher in HDWAC than in the other two colonoscopy groups (P=0.005).

In a number-needed-to-diagnose analysis, the number of HDWAC needed to detect one additional adenoma patient compared with SRSAC and HRSAC would be 6 (with adenoma detection on per-patient basis of 48.4%, 32.3% and 34.4%, respectively). Multivariate analysis with logistic regression found that the type of colonoscopy was the strongest independent predictor for flat adenoma detection. Other variables independently predicting polyp, adenoma and flat adenoma detection are shown in Table 4.

DISCUSSION

In this study, HDWAC detected more adenomas, flat adenomas, and adenomas with advanced histology <10mm in diameter compared with SRSAC and HRSAC.

Our findings are inconsistent with the results of a recently published study of 693 patients [16], which showed no difference in adenoma detection between HDWAC and SRSAC. In this series, however, adenoma prevalence and the mean number of adenomas detected per patient in HDWAC group was 26% and 0.43±0.87, respectively, which is approximately half the prevalence rate and adenoma detection reported in our study. Possible explanations for the difference might be either generally low adenoma prevalence in the population or insufficient quality of colonoscopic procedure performed by endoscopists with low adenoma detection in that study. It is, therefore, possible to speculate whether endoscopists with low adenoma detection would benefit from technical developments in colonoscopic technology, such as increased image resolution or wide-angle view. It is highly probable that rather than endoscopic resolution, the more important factor in attaining high adenoma detection is the operator technique, especially in less experienced endoscopists. Another study compared adenoma detection with high-definition and standard-definition endoscopes (both with 140° angle of view) in a population of 130 patients [17]. Although the mean number of adenomas per patient and the adenoma prevalence were by 30% and 11% higher in the

Table 3
The prevalence of adenomas categorised according to size, morphology, location, and histology

Patients with	SRSAC (n=254)	HRSAC (n=160)	HDWAC (n=93)	*P* value
≥1 adenoma, N (%)	83 (32.7)	54 (33.7)	45 (48.4)	0.02
<10 mm, N (%)	71 (28.0)	50 (31.3)	38 (40.9)	0.07
≥10 mm, N (%)	23 (9.1)	13 (8.1)	12 (12.9)	0.43
≥1 flat adenoma, N (%)	27 (10.6)	26 (16.3)	29 (31.2)	<0.001
<10 mm, N (%)	19 (7.5)	22 (13.8)	27 (29.0)	<0.001
≥10 mm, N (%)	10 (3.9)	6 (3.8)	6 (6.5)	0.53
≥1 polypoid adenoma, N (%)	65 (25.6)	37 (23.1)	25 (26.7)	0.77
≥1 right-sided adenoma, N (%)	45 (17.7)	35 (21.9)	28 (30.1)	0.04
≥1 left-sided adenoma, N (%)	55 (21.7)	36 (22.5)	27 (29.0)	0.36
≥3 adenomas, N (%)	15 (5.9)	11 (6.9)	9 (9.7)	0.47
≥1 adenoma <10 mm with advanced histology, N (%)	18 (7.1)	8 (5.0)	15 (16.1)	0.005

Table 4
Variables independently influencing the number of diagnosed polyps, adenomas and flat adenomas during endoscopy. As the variable "Examiner" in "All polyps" worsened the goodness-of-fit of the regression model, it was not included in the final model despite its statistical significance

	All polyps		Adenomas		Flat adenomas	
Variables	***B***	***P* value**	***β***	***P* value**	***β***	***P* value**
Colonoscopy type	-	0.05	-	0.07	0.16	<0.001
Age	0.22	<0.001	0.25	<0.001	0.14	0.001
Gender (male vs. female)	-0.22	<0.001	-0.24	<0.001	-0.14	0.001
Preparation (4 categories)	-	0.67	-	0.21	-0.12	0.007
Examiner (8 categories)	-	0.02	-	0.14	-	0.14
Indication (10 categories)	-	0.6	-	0.79	-	0.88

β – standardised coefficient beta

high-definition group, the difference was not statistically significant (*P*=0.20).

Two potential effects might have influenced adenoma detection in HDWAC group in our study. Firstly, the wide-angle instrument's capacity to expose more colorectal mucosa might have increased the overall adenoma detection by imaging adenomas on the proximal sides of the folds, predominantly in the right colon, which has a larger diameter with a higher chance for missing adenoma. Secondly, HD imaging might have enabled an increase in the overall adenoma detection by improved resolution of the colonic mucosa and, thereby, imaging subtle mucosal changes between the flat adenoma and the surrounding mucosa. This assumption is supported by the fact that the increase in the prevalence of adenomas in HDWAC group was primarily accounted for by increased detection of flat adenomas <10mm in diameter. Improvement in image resolution is not expected to increase the detection of protrusive or large adenomas, but rather of flat and small ones. This is supported by our findings of no difference in the detection of flat adenomas ≥10mm and polypoid adenomas of any size between the study groups.

The studies comparing endoscope withdrawal time and adenoma miss rate between wide-angle (170° or 210°) and standard-angle colonoscopy demonstrated a shortening of endoscope withdrawal time without compromising adenoma detection using a wide-angle instrument [9,10,27]. The endoscope withdrawal time did not differ between the groups in our study. Using HDWAC, we detected 0.91±1.27

adenoma per patient, whereas Rex et al [15] reported a detection of 1.8±2.2 adenoma per patient with white-light HDWAC. The quality of bowel preparation and the different experience level of endoscopists participating in our study might have negatively influenced adenoma detection rate. The difference between the endoscopist with the highest and lowest adenoma detection was threefold (data not shown). In one study, however, the variation in adenoma detection was reported to be over tenfold between 12 experienced endoscopists [28].

Adenomas with HG IEN or villous morphology carry a higher risk of progression to carcinoma [29]. In our study, a significantly higher proportion of patients with ≥1 adenoma with advanced histology <10mm in size was in the HDWAC group. In contradiction to this, the prevalence of adenomas with advanced histology ≥10mm did not differ between the study groups (data not shown). The impact of HDWAC on the detection of high-risk adenomas is of clinical importance since missing them may lead to interval CRC development. Although a not statistically significant yet potentially clinically important increase in the number of patients with ≥3 adenomas was seen in the HDWAC group, since these patients are at high risk for the development of advanced neoplasia during the follow-up [30].

There are limitations to our study. As the study was non-randomised and the allocation depended on the availability of the instrument only, selection bias is possible. Nevertheless, the same demographics, colonoscopy indications, and quality of bowel preparation in all groups indicate that the groups were well matched. Different adenoma detection and different numbers of colonoscopies performed by each endoscopist in the study groups were further potentials for biases. On the other hand, our results probably reflect more accurately the true diagnostic yield of the studied technique when performed in the conditions of routine practice. Finally, the colonoscopists were not blinded to which instrument they were using, which might have led to a more precise inspection of the colonic mucosa in the HDWAC group.

In conclusion, this study has shown the benefit of HDWAC for colorectal adenoma detection, when a sufficiently long withdrawal interval is kept. The increase in overall adenoma detection was primarily accounted for by the increase in the detection of adenomas, including flat adenomas and adenomas with advanced histology, which were <10mm in size. HDWAC might be useful in decreasing the risk of interval CRC development within a short term after clearing or negative colonoscopy by detecting small neoplastic lesions with advanced histology. These findings support the use of HDWAC in clinical practice, but these results should be interpreted with caution because of the study design and other limitations mentioned. More randomised controlled studies are needed to clearly establish the role of HDWAC in current practice.

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CLINICAL APPLICATION OF ELECTROGASTROGRAPHY

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KEY WORDS

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ABSTRACT

Electrogastrography (EGG) is a completely non-invasive measurement of the gastric myoelectrical activity from cutaneous Ag\AgCl electrodes placed on the abdominal wall anterior to the stomach. EGG can be recorded from a pair of electrodes for a single or for multiple channels.
The advantages of four-channel EGG measurement consist in detailed analysis; it also allows the study of electrical coupling and propagation of gastric slow-wave activity.
The study consists of a 45 minutes' preprandial period and a 45 minutes' postprandial period after consumption of a standard meal.
In health, the dominant frequency and power reflect the normal basic rhythm of the slow waves, and the contractile activity provoked by food or other stimuli. The peristaltic antral activity that is essential for normal primary gastric function is reflected in EGG as an increase in its dominant power. The impaired myoelectrical activity observed in EGG is associated with disturbed motility and upper gastrointestinal symptoms, and may be suggestive of delayed gastric emptying.

INTRODUCTION

Electrogastrography methods have been used in many clinical studies over the past 80 years. In 1922 Alvarez predicted that electrical abnormalities of the stomach might be related to gastrointestinal symptoms and abnormal gastric function. In 1980 antral dysrhythmias were recorded with mucosal electrodes in a series of patients with unexplained nausea and vomiting.
The electrical activity of the stomach can be subdivided into two general categories: electrical control activity (ECA) and electrical response activity (ERA).
ECA is characterised by regularly recurring electrical potentials, originating in the gastric pacemaker located in the great curvature of the stomach and sweeping in an annular band with increasing velocity towards the pylorus. ECA is not associated with contraction of the stomach unless coupled with

action potentials, referred to ERA. The usual practice is to record the EGG signal from several cutaneous electrodes and to select the signal with the highest amplitude for further analysis (Fourier spectral analysis). The EGG is usually evaluated in terms of changes in EGG amplitude and frequency.

Abnormal myoelectrical activity can be detected in many patients with delayed gastric emptying, those who may show abnormally rapid rhythm (tachygastria), abnormally slow rhythm (bradygastria), or no increase in signal amplitude after a meal. Similar changes have been reported in patients with delayed gastric emptying associated with reflux disease or anorexia nervosa, with functional dyspepsia, patients after surgical resections (with Billroth II anastomosis). Another group consists of the so-called pseudo-obstruction – such as scleroderma, amyloidosis, and muscular dystrophies.

One of the most common causes of delayed emptying is diabetes, although many diabetics have neuropathy, mainly autonomic neuropathy.

The symptoms include bloating, distension, nausea, and vomiting.

METHODS

Gastric electrical activity was recorded from 4 surface electrodes placed on the upper abdomen.

The signal that will be recorded by electrogastrography is very weak and needs to be amplified, filtered, and digitised before it can be stored either online onto a computer or in a separate recording device. In order to obtain an EGG recording with a high signal without any "noise" care must be taken in preparing the skin of the abdomen where percutaneous electrodes should be placed. The places should be cleaned and abraded with some sandy skin preparation jelly in order to reduce the impedance below 10 KΩ. To reduce severe motion artefact we use what is called a motion sensor. The most common placement of electrodes for a four-channel recording is shown in Figure 1. Several electrodes are placed along the curvature of the stomach. EGG should be recorded in a quiet room to minimalise the risk for artefacts and the patient needs to stay as quiet as possible to minimalise their movements during the study.

The processing of the measurement starts after an overnight fasting; the patient is positioned in a supine or semireclining position. After 45 minutes' fasting recording (preprandial), the 10 minutes' period is followed by a standardised test meal plus drink (including at least 200 kcal of energy; the meal should be mainly solid food) and then a 45 minutes' feed period recording (postprandial).

Numerical analysis usually includes transformation of the curve into frequency components using Fourier transforms or a similar technique. Reliable data can be obtained using a recording apparatus set for a frequency range of 0.5 to 9 cpm, and an amplitude of 50 to 500 μV, to encompass a broad range of dysrhythmic patterns. For practical purposes, we will focus on the ambulatory device which we use: Digitrapper EGG; Synectics Medical Inc.

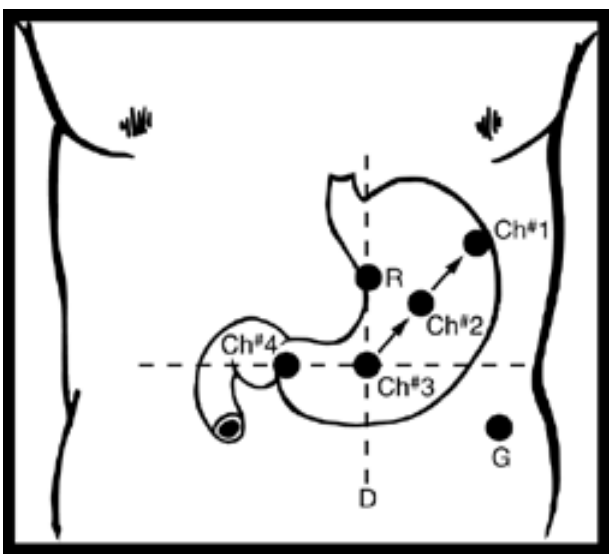

Figure 1
Position of electrodes on the abdomen
Ch 1–4: electrodes; R, reference electrode; G, ground

INDICATIONS

Unexplained nausea or vomiting
Suspected or confirmed gastroparesis
Functional dyspepsia
Monitoring pharmacologist therapy

ANALYSIS

Data collected during the recordings are analysed to obtain major EGG parameters. The clinical application of an EGG measurement consists in the understanding of these parameters and their patterns in different groups:

- Dominant frequency: The EGG dominant frequency reflects the frequency of the gastric slow waves (frequency of gastric pacemaker). The recordings obtained from hundreds of human subjects indicate a normal frequency range of 2.5–3.7 cpm.
- Dominant power: The dominant power of EGG is associated with the amplitude and regularity of EGG. The absolute value of the power is influenced by a number of factors (e.g., thickness of the abdominal wall,

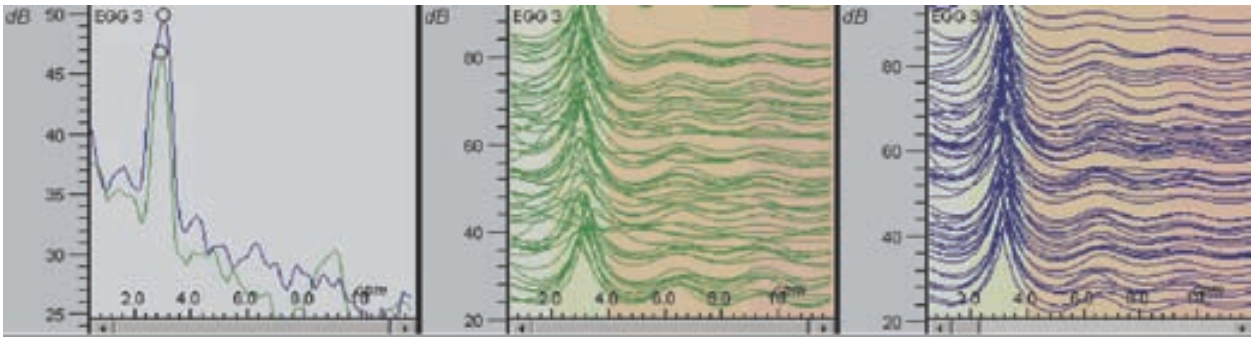

Figure 2
Spectral analyses of the electrogastrogram (EGG)

electrode configuration, recording devices), and thus, only relative changes are considered (e.g., before and after stimulation).

- Percentage of normal slow waves: The percentage of the normal slow waves reflects the regularity of EGG. It is defined as the percentage of time during which 2.5–3.7 cpm slow waves are present across the entire recording.
- Percentage of gastric dysrhythmias: The percentage of dysrhythmias reflects the time during which 2.5–3.7 cpm slow waves are absent across the entire recording. They are classified according to their peaks in the range of frequency: bradygastria (0.5–2.5 cpm), tachygastria (3.8–9 cpm), and arrhythmia (during which no dominant peak can be identified in the range of 0.5–9 cpm).
- Percentage of SW coupling: the percentage of time during which the SW was determined to be coupled.

Gastric dysrhythmias have often been reported in patients with motility disorders, but only seldom in normal subjects with no history of gastrointestinal motility diseases. Several studies have shown that EGG can be used to differentiate between normal subjects and patients with gastroparesis (75 % of whom have EGG abnormalities). Typical EGG abnormalities in patients with such motility disorders include:

– deterioration of EGG after a test meal, which is shown as a decrease in EGG power;
– absence of normal slow waves;
– gastric dysrhythmias (including bradygastria, tachygastria, and arrhythmia).

DISCUSSION

Slow waves (SW) determine the frequency and the direction of propagation of the contractions. The corresponding EGG parameter, the dominant frequency, equals that of the internal measurement. In previous studies, Abell et al. and other investigators found that the EGG's dominant frequency is of gastric origin, and matched the gastric slow waves in mucosal tracings. These findings were reproduced in other experiments using serosal and cutaneous electrodes simultaneously. The correlation between gastric contractions and the EGG's dominant power was investigated by internally recording the myoelectrical activity.

A postprandial increase in EGG power is often observed and is thought to be attributable to increased slow-wave amplitude and spikes during gastric contractions. The explanation of the postprandial power increase is still debatable. Some investigators think that it reflects the physical distension of the stomach and the subsequent movement of the pacemaker closer to the surface. However, ultrasonographic measurement of the distance between the gastric and abdominal walls, before and after meals, did not support this theory. Gastric contractions remain the main reason for the postprandial power increase.

Dysrhythmia is associated with symptomatology and hypomotility (the existence of hypomotility is proved by simultaneously performing manometry). Gastric dysrhythmia has long been shown to reflect disturbed gastric motility in a variety of states including pregnancy, motion sickness, and diabetic gastroparesis. In the nausea and vomiting associated with pregnancy, dysrhythmic recordings disappear after delivery, along with the symptoms. Experimental induction of motion sickness induces symptoms and dysrhythmia, and diabetic gastroparesis reflects the same association with known hypomotility.

Tachygastria (including frequencies from 3.75 to 10.0 cpm) originates mostly from an antral ectopic source with retrograde propagation, whereas bradygastria may be either from a normal or an abnormal source. Tachygastrias are evoked by loss of vagal parasympathetic activity and/or increase in the sympathetic nervous system. An interesting study showed the normalisation of dysrhythmic patterns reflected in EGG, after a prokinetic treatment, with a similar decrease in symptoms.

The correlation between gastric emptying and myoelectrical activity has always been of great interest to investigators in the clinical field. Although myoelectrical activity controls motility, there are some factors that affect gastric emptying but cannot be appreciated in EGG, such as pyloric stenosis.

Diabetic autonomic neuropathy is considered to be quite a common complication of diabetes mellitus. It usually remains silent for a long time, without clinical signs, and therefore it has been seldom diagnosed and treated. Diabetic autonomic neuropathy significantly rises mortality rates in patients suffering from this disorder. All tissues with autonomic innervation can be affected. Autonomic neuropathy is present in the cardiovascular system as well as in the gastrointestinal and urogenital tracts. It has been suggested that, in patients with diabetes mellitus-based gastric dysrhythmias, it may contribute to disordered gastric motility and dyspeptic symptoms. In diabetic patients studied under euglycemic condition the incidence of dysrhythmias was found to be not higher than in healthy controls.

Most commonly, diabetes is associated with gastroparesis. It is defined as a chronic disorder of gastric motility as evidenced by delayed gastric emptying of solid meals.

CONCLUSIONS

EGG is a non-invasive technique which yields information about the gastric myoelectrical activity. This information is different from that obtained by manometry, barostat studies, and gastric emptying tests.

The applications of EGG are in two main areas. The first is assistance in the clinical evaluation and diagnosis of patients with gastric motility disorders. The other is determination of the gastric response to some stimuli (caloric, exogenous or pharmacological).

The study of the propagation of the gastric slow wave represented by multichannel recording may provide additional information related to the occurrence of real-time events in different parts of the stomach and the spatial coordination. Multichannel recordings have been somewhat overlooked in the past but certainly have the potential to enhance EGG comprehensibility.

Electrogastrography is not only of great clinical significance in diagnosing gastric motor disorders, but may also provide a therapeutic approach. Recently, experiments in gastric pacing (electrical stimulation) have been conducted, including a multicenter study. Promising results have been shown in the improvement of gastric emptying and symptoms in patients with gastroparesis refractory to medical therapy. EGG could be an important screening test in the evaluation of patients with suspected gastroparesis. In the future EGG could be used as a follow–up investigation for monitoring treatment and to assess the relationship between EGG and clinical changes.

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ABDOMINAL ULTRASOUND ACCURATELY DETECTS COMPLICATIONS IN PATIENTS WITH HEPATICOJEJUNOANASTOMOSIS

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ABSTRACT

Hepaticojejunoanastomosis is a surgical replacement of the biliary tract. The most frequent indications for this procedure are biliary duct injuries, other benign biliary tract stenoses, biliary tumours, choledochal cysts, and biliary atresia in children. The main complication of this method is stenosis of the anastomosis.

We retrospectively reviewed the cases of eight patients with a history of hepaticojejunoanastomosis for benign disorder with a view to the role of ultrasound examination in their follow-up. All eight patients had hepaticojejunoanastomosis-related complications during the follow-up. Abdominal ultrasound was used as a primary diagnostic modality in the follow-up of all patients. When a complication was suspected, it was followed directly by an invasive therapeutic method (PTD, ERC, drainage); in four patients there were further non-invasive diagnostic tests indicated. Further non-invasive tests did not provide any new information, they only confirmed the ultrasound findings. If the clinical picture, laboratory tests, and ultrasound examination were taken together, we were able to accurately detect complications in all patients.

According to our results we can conclude that abdominal ultrasound is an accurate method for the detection of hepaticojejunoanastomosis-related complications and should be preferred in the surveillance of these patients.

INTRODUCTION

Hepaticojejunoanastomosis is a surgical replacement of the biliary tract; it is constructed on the excluded first jejunal loop according to Roux, or in Tondelli's modification, in which the length of the afferent bowel loop is a minimum of 60 cm [1]. The anastomosis should be as wide as possible. While constructing the anastomosis, the surgeon should suture the intestinal mucosa with the biliary mucosa with single non-absorbable stitches. If the biliary pathways are too gracile, a silicon drain (also called "lost drain") can be used for the

Table 1
The indications for hepaticojejunoanastomosis and the length of follow-up

Patient	Indication for hepaticojejunoanastomosis	Length of follow-up (years)
No. 1	Iatrogenic injury of the common bile duct during laparoscopic cholecystectomy	7
No. 2	Iatrogenic injury of the common bile duct during laparoscopic cholecystectomy	3
No. 3	Distal common bile duct stenosis as a complication of chronic pancreatitis	11
No. 4	Mirizzi's syndrome with duodenal diverticulum	12
No. 5	Iatrogenic injury of the common bile duct during laparoscopic cholecystectomy	6
No. 6	Hepaticolithiasis as a complication of iatrogenic lesion during cholecystectomy	6
No. 7	Treatment of choledochal cyst in childhood	8
No. 8	Iatrogenic injury of the common bile duct during open cholecystectomy	4

Table 2
Complications and final treatment

Patients	Hospitalisation for cholangitis	Stenosis of the anastomosis	Other complications	Concomitant diseases	Final treatment of complications
No.1	1	NO	Spondylodiscitis	Arterial hypertension	Intravenous ATB therapy
No. 2	3	YES	Impacted "lost" drain	Operation of herniated intervertebral disc L5–S1	New side-to-side hepaticojejunoanastomosis according to Hepp-Couinaud
No. 3	8	YES		Chronic pancreatitis	Transient PTC/PTD with dilation
No. 4	2	NO		Thyroid hypofunction	Transient PTC/PTD
No. 5	4	YES	Septic shock with respiratory failure	Obesity, Paranoid schizophrenia	Transient PTC/PTD with dilation
No. 6	1	NO	Hepaticolithiasis	Acute biliary pancreatitis (twice)	Intravenous ATB therapy
No. 7	2	NO	Hepaticolithiasis	Chronic pancreatitis	Transient PTC/PTD
No.8	3	NO	Multiple liver abscesses	Arterial hypertension, Diabetes mellitus	CT with drainage

construction of the anastomosis [2, 3]. In these cases the drain is spontaneously passed into the jejunal lumen and subsequently lost in the stools.

The most frequent indications for this operation are primarily biliary duct injuries that can occur as a complication of cholecystectomy [4–8], both open (0.2–0.3 %) [9, 10] and laparoscopic (0.3–0.8 %) [11, 12], followed by other benign biliary tract stenoses [13, 14], some biliary tumours [15, 16], and biliary atresia in children. It is also used in the treatment of choledochal cysts [17–19], mainly types I-IV according to the Todani classification [20].

The main complication of this method is stenosis of the anastomosis [21–23]; it can develop in 25 % of cases [24]. The stenosis of the anastomosis usually presents as a recurrent cholangitis, cholestasis with development of jaundice and elevation of cholestatic liver enzymes. These stenoses need to be solved by ERC (Endoscopic Retrograde Cholangiography) with dilation and/or a biliary stent placement or PTC/PTD

Table 3
Recommendations for ultrasonographists

Hepaticojejunoanastomosis itself	Intestinal loop edging to the liver hilus (better view in patient's left side position)	
Bile ducts	Width (normal width of the intrahepatic bile ducts is up to 4 mm)	
	Aerobilia – a sign of anastomosis patency (hyperechoic bodies or spots with just an intimated acoustic shadow)	
	Hepaticolithiasis (hyperechoic bodies with a strong acoustic shadow)	
	Drains if present	
Liver parenchyma	Normal / Cirrhosis, and/or signs of portal hypertension	
	Focal lesions if present	Cholangiogenic liver abscess – single/ multiple
		Hepatocellular carcinoma in cirrhosis
Free fluid	If present	

(Percutaneous Transhepatic Cholangiography and Drainage); in a few cases surgical repair is necessary [25].
During the follow-up of patients with hepaticojejunoanastomosis we can use clinical examinations, laboratory tests and, finally, imaging methods. Of these, abdominal ultrasound is considered to be the most convenient for its non-invasiveness and accessibility.
We have decided to evaluate the role of ultrasound examination in the follow-up of our group of eight patients with a history of hepaticojejunoanastomosis for benign disorder. We did not include patients with malignant disorders (cholangiocarcinoma) because of their worse prognosis and survival [26–29].

MATERIALS AND METHODS

We retrospectively reviewed the cases of eight patients with a history of hepaticojejunoanastomosis in the surveillance in our gastroenterological outpatient clinic. The main point was the role of abdominal ultrasound in the follow-up of these patients.
Our group of patients consisted of two men and six women aged 40–83 years (mean age 57 years). The indications for hepaticojejunoanastomosis and the length of the follow-up of all patients are mentioned in Table 1.
In five patients the operation was performed at a tertiary centre with extensive experience in biliary surgery; in three patients the operation was performed in a local hospital. The construction of hepaticojejunoanastomosis during the primary operation was performed in one case only (in a local hospital).
We evaluated the position of ultrasound examination in non-invasive imaging methods used in these patients and the accuracy of its findings.

RESULTS

The complications and final treatment are presented in Table 2.
Abdominal ultrasound was used in the follow-up of all eight patients; in all patients it was followed directly by an invasive method (PTD, ERC, drainage), in four patients (No. 5, No. 6, No.7, No.8) there were further non-invasive tests indicated (MRC, CT, choledochoscintigraphy). Further non-invasive tests did not provide any new information, they only confirmed the ultrasound findings (liver abscess confirmed on CT, liver abscess excluded on CT, hepaticojejunoanastomosis with suspected stenosis described on MRC, cholescintigraphy showed prolonged evacuation time and persistent activity in left liver lobe – hepaticolithiasis on ultrasound).
If the clinical picture, laboratory tests, and ultrasound examination were taken together, we were able to accurately detect complications in all patients.
In our group there was no patient with a non-complicated course. Morbidity was 100 %. Stenosis of the anastomosis developed in three patients (37.5 %) and was treated by PTC/

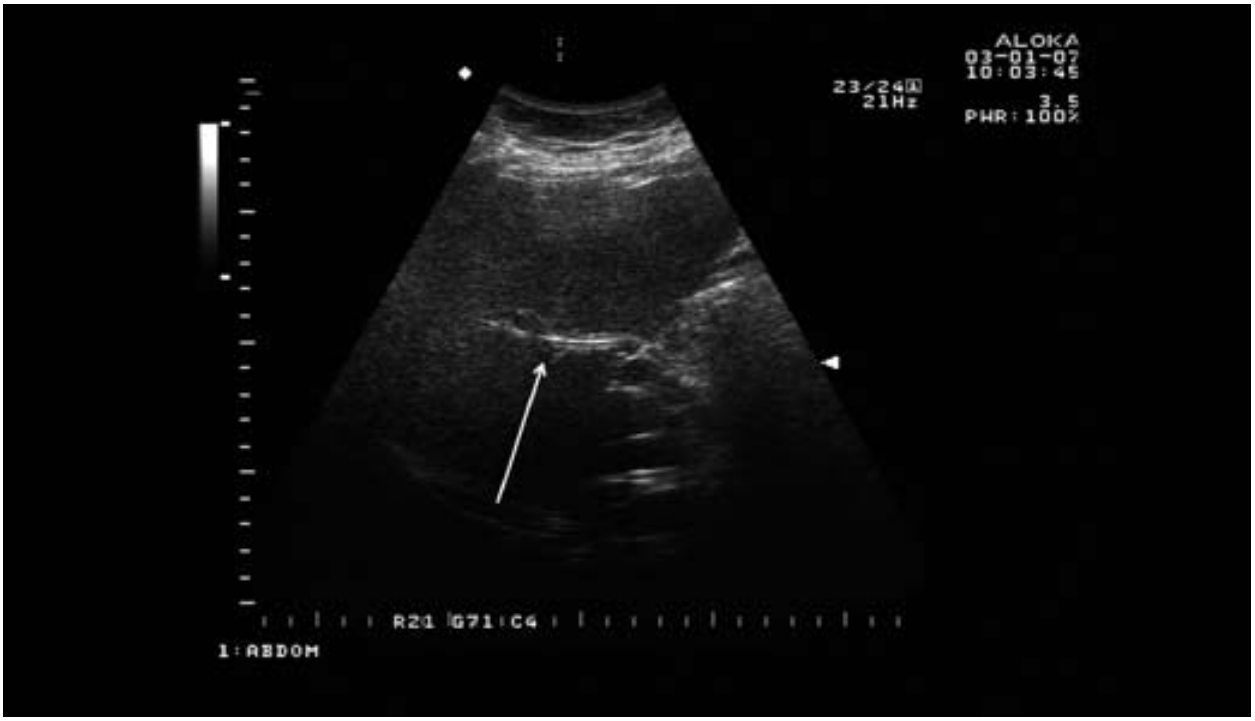

Figure 1
"Lost" silicon drain in intrahepatic biliary pathway

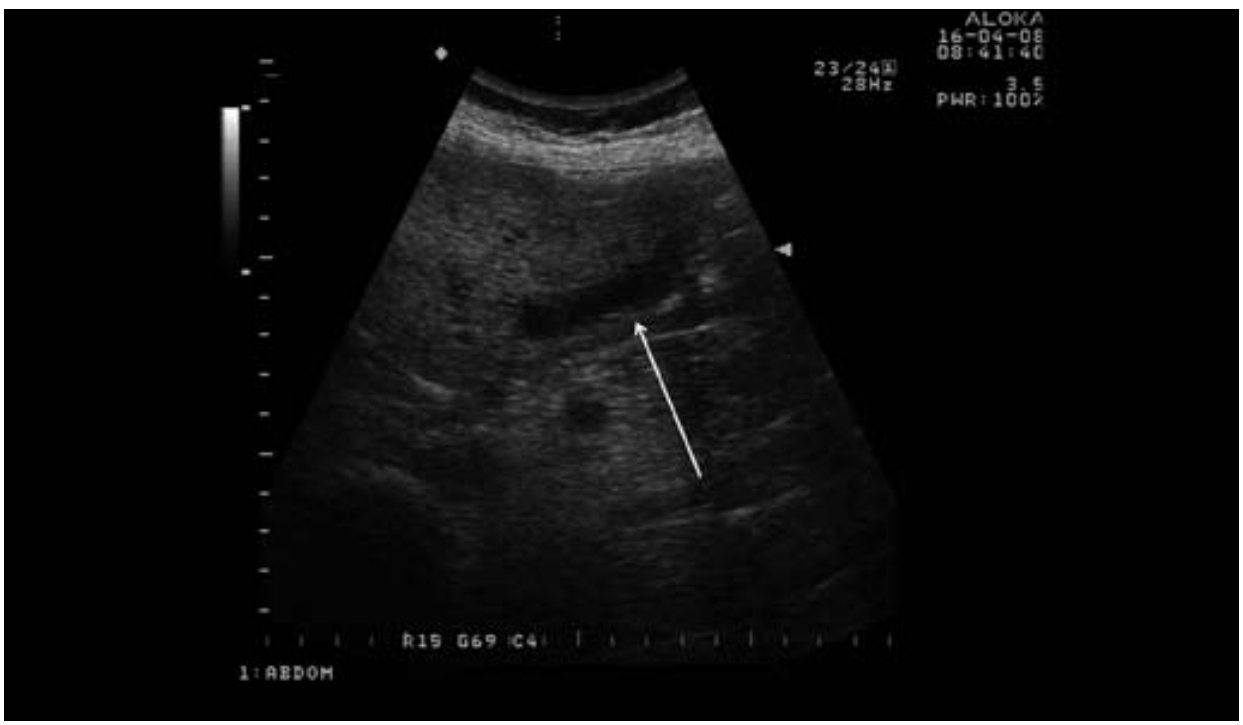

Figure 2
Bowel loop edging to the liver hilus

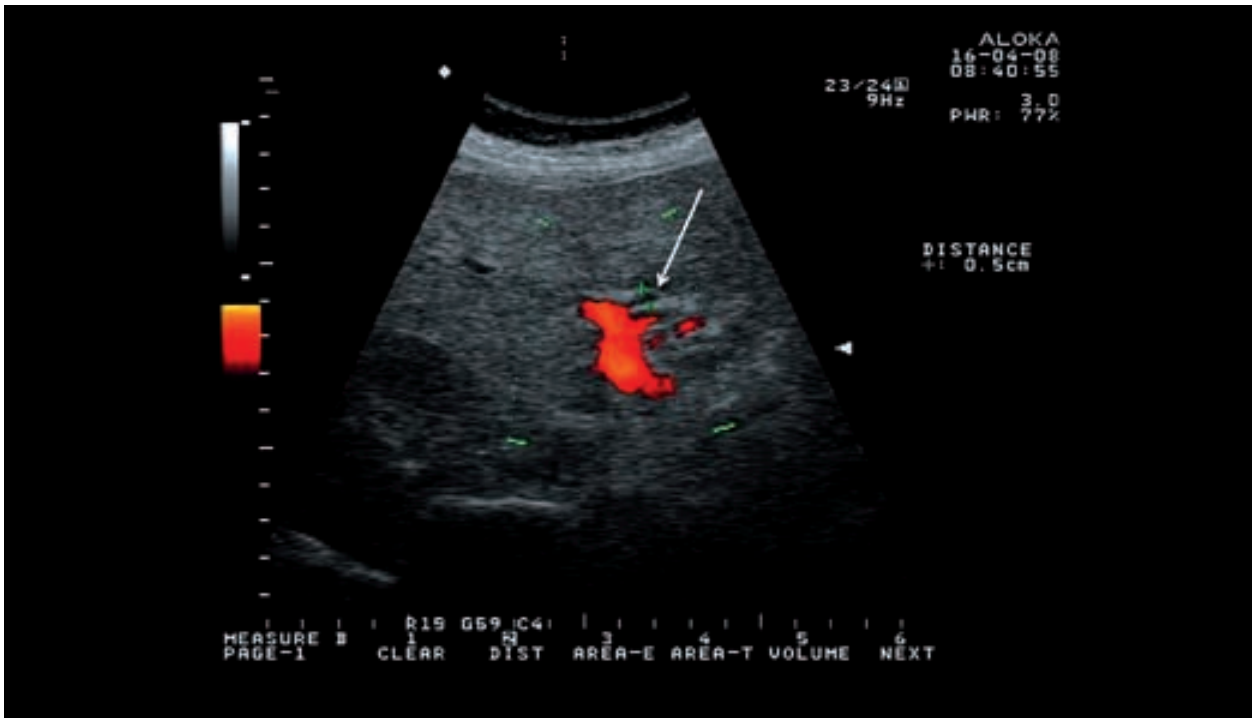

Figure 3
Hepaticojejunoanastomosis: measurement of the width of the intrahepatic bile ducts

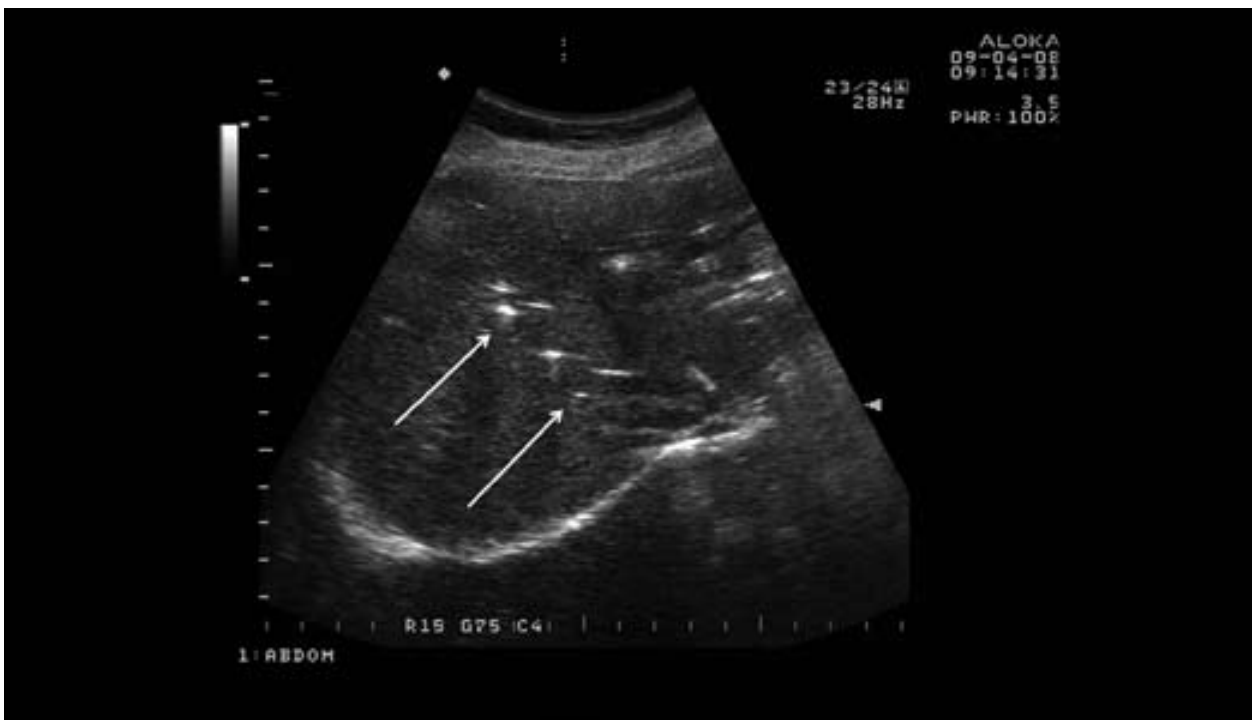

Figure 4
Aerobilia as a sign of anastomosis patency

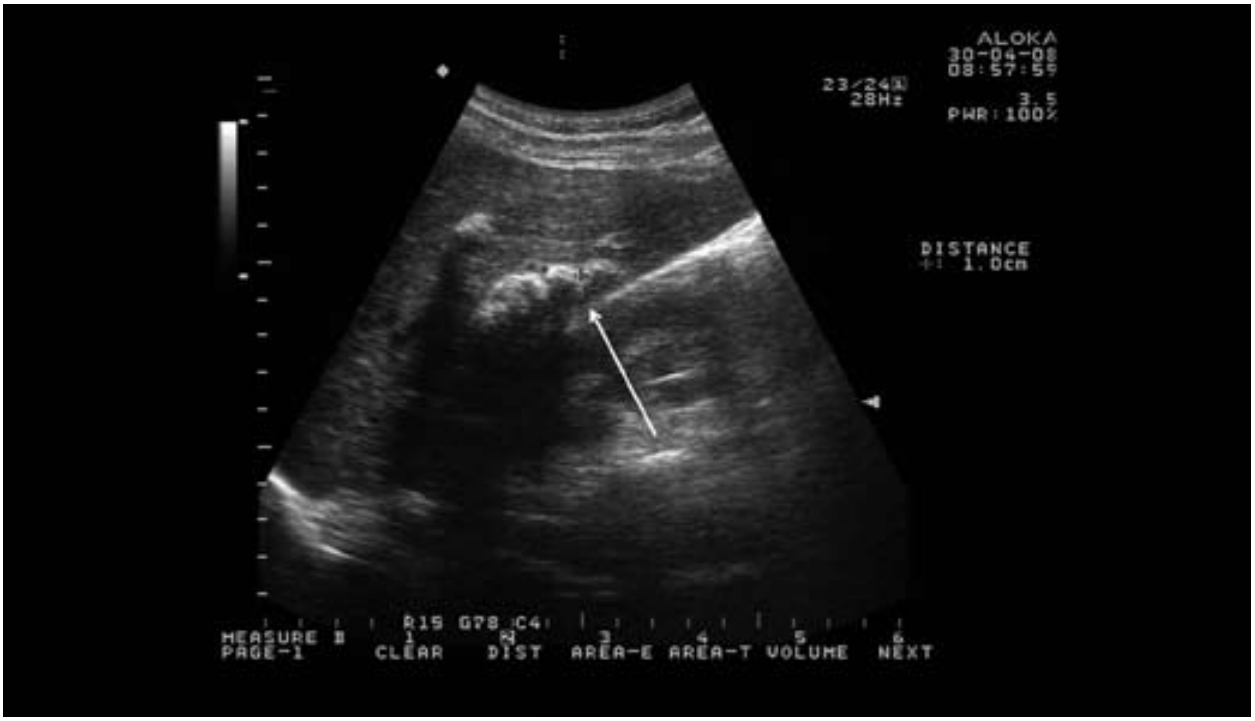

Figure 5
Hepaticolithiasis: hyperechoic bodies with a strong acoustic shadow

PTD with dilation in two cases (No. 3, No. 5); in patient No. 2 surgical repair was necessary.

After a complicated laparoscopic cholecystectomy in 2003 with a common bile duct injury in patient No. 2 solved by follow-up hepaticojejunoanastomosis two days later, the anastomosis was constructed on a silicon ("lost") drain. Since 2006 there had been frequent attacks of cholangitis. On abdominal ultrasound there was a shadow of the silicon drain in the biliary pathways described – impacted "lost" drain, which was the cause of recurrent cholangitis (Figure 1). The ERC and PTC/PTD were not possible, this patient underwent double-balloon ERC (the first double-balloon ERC in the Czech Republic, Faculty Hospital Hradec Králové, December 2006), extraction of the drain was impossible due to a severe stenosis of the anastomosis. The final treatment was a surgical resection of hepaticojejunoanastomosis with the "lost" drain and a construction of the new side-to-side hepaticojejunoanastomosis according to Hepp-Couinaud. The patient is under surveillance, to date with no other complications. In this case the lost drain was only visible on ultrasound and nearly invisible due to its low radiopacity on X-ray examination.

The abdominal ultrasound was used as a primary diagnostic modality in each case. It described accurately the impacted drain, hepaticolithiasis, and liver abscesses. In the case of cholangitis, abdominal ultrasound accurately described the width of the biliary pathways (crucial for subsequent PTC/PTD), and it confirmed or excluded the presence of liver abscess.

DISCUSSION

Physicians performing ultrasonography in patients with hepaticojejunoanastomosis should focus their attention on the anastomosis itself (Figures 2, 3) and also on the detection of possible complications. The width of intrahepatic biliary pathways should be measured and any presence of aerobilia described. An indispensable part of the examination is represented by a careful inspection of liver parenchyma (structure, focal lesion) and the evaluation of portal hypertension signs and free fluid in the abdominal cavity.

Recommendations for ultrasonographists are mentioned in Table 3.

Abdominal ultrasound in patients with hepaticojejunoanastomosis is an examination with many pitfalls. The lucidity of the subhepatic region could be impaired by the presence of gas and bowel loop adhesions. The examiner must be aware of the presence of foreign bodies, for example drains and clips, and the possibility of other concurrent disease should be counted in.

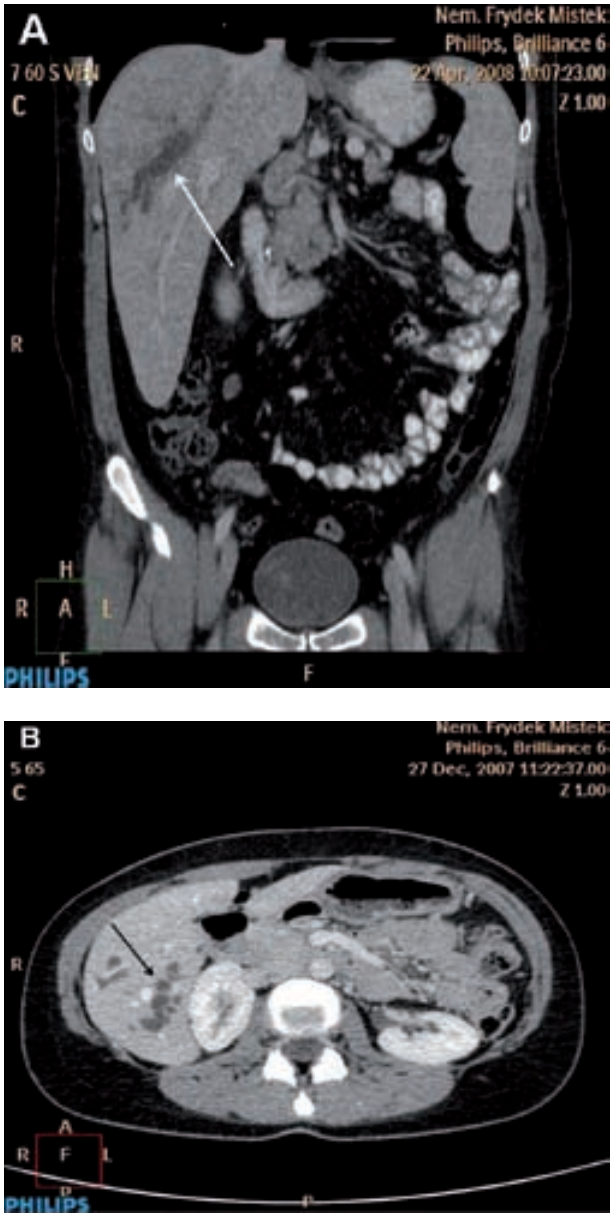

Figure 6
Hepaticolithiasis on a CT scan: intrahepatic biliary duct dilation, coronal (A) and axial (B) images

However, abdominal ultrasound remains the only imaging method that we can perform in all patients with hepaticojejunoanastomosis and the knowledge of the proper examination of these patients is crucial. In the majority of patients we cannot use ERC because of changed anatomy; in some of them the examination has lately become possible due to the so-called double-balloon ERC [30–33], but this method is not widely available except for a few centres. In patients without dilation of the intrahepatic bile ducts PTC/PTD is also an inconvenient imaging method and should not be done only for diagnostic purposes. In all of these patients accurate ultrasound examination can lead us directly to the appropriate therapeutic method selection.

There are a few findings that the examiner can be encountered with. Frequently aerobilia (Figure 4) is present and is usually considered as a sign of an anastomosis patency. Sometimes it can be confused with hepaticolithiasis (Figure 5), which is also common in these patients. Both aerobilia and hepaticolithiasis portray as hyperechoic bodies along the biliary pathways, but aerobilia has just an intimated acoustic shadow in contrast to hepaticolithiasis, which has a very strong acoustic shadow. Hepaticolithiasis can complicate stenosis of the anastomosis; however, it could also result from a primary disease (i.e. Caroli's disease) [34, 35]. As a prevention of lithiasis ursodeoxycholic acid therapy is recommended [36, 37]. We can also use a CT scan for hepaticolithiasis detection, but CT shows us just the intrahepatic biliary duct dilation, not hepaticolithiasis itself like ultrasound (Figure 6) [38, 39].

Another typical ultrasound finding is a cholangiogenic liver abscess (Figure 7), both single or multiple [40, 41]. The discovery of a hepatic abscess should always call our attention to possible stenosis of the anastomosis. If the stenosis is left unsolved, subsequently a secondary biliary cirrhosis [42, 43] with its typical ultrasound signs (Figure 8) can develop. Secondary biliary cirrhosis is a very serious complication of hepaticojejunoanastomosis, and it is a respected indication for liver transplantation [44, 45].

CONCLUSIONS

According to our results we can conclude that abdominal ultrasound is an accurate method for the detection of hepaticojejunoanastomosis-related complications and should be preferred in the surveillance of these patients. It enables us to directly select an appropriate invasive treatment method.

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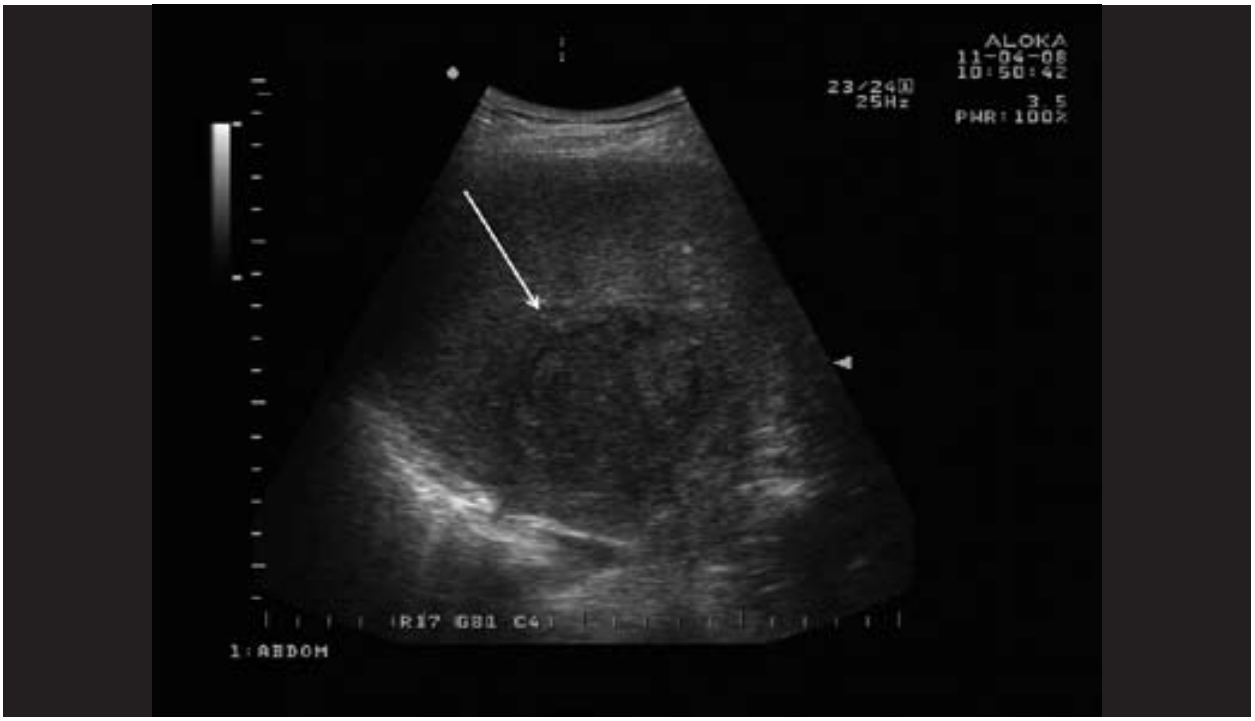

Figure 7
Liver abscess usually portrays as an inhomogeneous lesion; it can be both hyperechoic and hypoechoic

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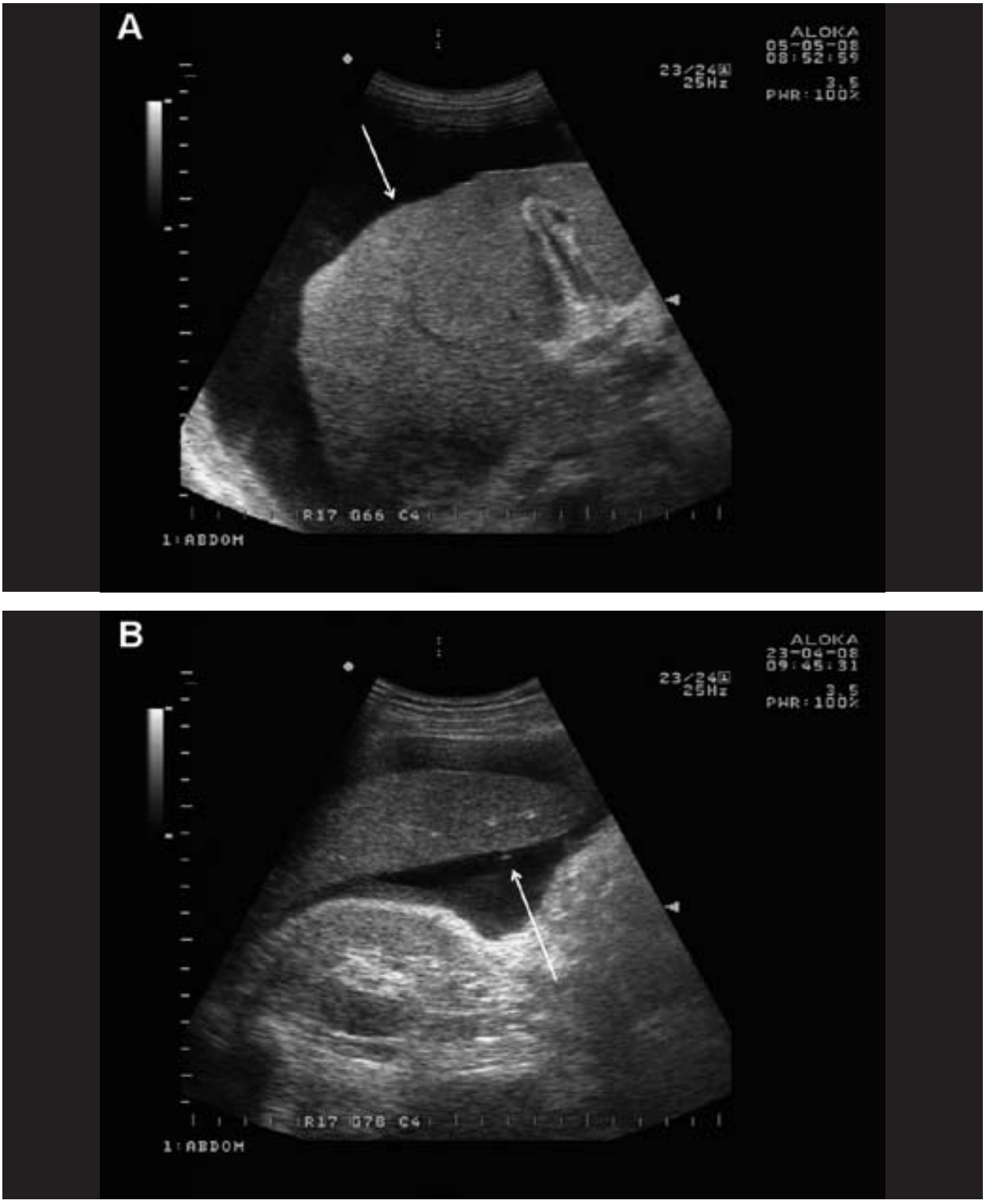

Figure 8
Ultrasound signs of liver cirrhosis: granular structure of the liver parenchyma, irregular surface of the liver (A), liver parenchyma, ascites (B)

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ACUTE PANCREATITIS AS A FIRST SYMPTOM OF PANCREATIC CANCER IN A DIFFUSE AUTOIMMUNE PANCREATITIS PATIENT

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INTRODUCTION

Autoimmune pancreatitis (AIP) is a unique form of chronic pancreatitis that can be defined as a chronic inflammation of the pancreas due to an autoimmune mechanism showing in most of the cases reversible improvement of pancreatic morphology and function with oral steroid therapy [1]. AIP represents 4 % to 6 % of all chronic pancreatitis cases [2]. AIP can be divided into two forms – focal and diffuse. The focal form of autoimmune pancreatitis, also called mass-forming pancreatitis, is found in the head of the pancreas in about 80 % of all cases; therefore it can be easily misdiagnosed from adenocarcinoma [2, 3]. However, there are no references reporting on the presence of adenocarcinoma in the diffuse form of AIP [4].

We report on a case of a male patient with diffuse form of AIP, with a relatively short history of clinical symptoms, complicated by invasive ductal pancreatic adenocarcinoma with fatal clinical outcome.

CASE REPORT

A 40–year-old man, complaining of slight pressure pain in the abdomen for several years, was admitted to another local hospital in summer 2005 for painless icterus. The ERCP (endoscopic retrograde cholangiopancreatography) revealed a stenosis (of 2 cm in length) of the distal choledochus with prestenotic dilatation. It was solved by duodenobiliary drainage (DBD). Examinations were then completed in autumn 2006 in FHB (Faculty Hospital Brno). MRI (magnetic resonance), CT (computed tomography), and EUS (endoscopic ultrasonography) were performed, showing the typical sausage-like morphology of the pancreas. The level of IgG4 was found to be elevated: 1, 9 (0.07–1.4), the levels of the oncomarkers (CEA, Ca 19–9) were normal (as well as 4 times during the whole follow-up of the patient). A diagnosis of diffuse form of AIP was assumed. Mutational analyses of SPINK, PRSS, and CFTR genes were negative. The patient received corticoids (40 mg

per day) for one month, and then in decreased dosage until they were discontinued. In summer 2006 diabetes mellitus was diagnosed with the necessity of intense insulin regime. The findings did not change even after corticoid treatment – that is why EUS-guided fine needle aspiration (FNA) was performed in October 2006. Aspirate preparations contained almost exclusively finely and coarsely granular necrotic debris intermingled with numerous neutrophils. Several sheets of ductal epithelial cells with no signs of dysplasia and some inconspicuous acinar cells were revealed. Even though the performance of FNA was uneventful, a severe acute pancreatitis developed within 3 days, when the patient was again admitted to hospital. Abdominal ultrasound as well as CT showed a formation at the head of the measuring of 6x5x4cm and the diagnosis of advanced generalised pancreatic tumour was made. The suggested oncological palliative treatment was not carried out owing to the patient's bad condition. Afterwards, the patient was repeatedly admitted to our clinic and died in March 2007.

Autopsy revealed extensive infiltration of the pancreatic head with structures of moderately differentiated ductal adenocarcinoma, spreading into the peripancreatic fatty tissue, with infiltration of omentum, with multiple metastases in vertebral bodies (L1 and L3), in the liver and lymph nodes (peripancreatic, in the porta hepatis, and along the abdominal aorta).

DISCUSSION

Chronic pancreatitis (CP) is usually defined as a progressive process that leads to the destruction of the parenchyma and to exocrine and terminally also endocrine insufficiency [5,6,7,8]. Its incidence in our country – although the data are from the 1980s they are still true – is 7.9 for 100 000 inhabitants per year; the rest of Europe is mostly the same: 7–10 for 100 000 inhabitants per year [9,10,11].

Chronic pancreatitis can be classified from many views; we use the TIGAR-O classification system of the risk factors associated with CP, which was published in 2002. It divides the patients into groups by aetiology – therefore it is very simple and practical. It can also predict the course of the disease and approximately the risk of pancreatic cancer. The TIGAR-O means: T for toxic-metabolic, I for idiopathic, G for genetic, A for autoimmune, R for recurrent and severe acute pancreatitis, and O for obstructive form [5]. Autoimmune pancreatitis. The first references on CP in connection with some other autoimmune disease come from the middle part of the last century (1950 – Ball connection with ulcerative colitis). There are two basic units: diffuse form (called sausage-like) enlargement of the whole pancreas, with hypervascularisation, segmental or diffuse narrowing of the main pancreatic duct, etc. The focal form – as mentioned before, also called mass-forming pancreatitis, is found in the head of the pancreas in about 80 % of all cases.

For the typical morphology of the diffuse form, CT, MRCP or EUS can be easily used for the diagnosis. Other important factors to be observed are the set of antibodies (like ASMA, RF, ANA, IgG4, anticarbonyl anhydrase, etc.). Unfortunately, there is none sufficient for the pancreas and there may also be geographical diversity. The inflammatory infiltrate consists mainly of lymphocytes and plasma cells, but it also contains some macrophages and occasionally also neutrophilic and eosinophilic granulocytes. AIP can be also divided into two forms: isolated and associated with other systemic disease (like DM, PSC, SS) [12,13].

Acute necrotising pancreatitis does not represent a typical complication of AIP. Clinical symptoms are variable and most commonly include painless jaundice [13], weight loss, and abdominal pain -commonly mild and variable in duration, usually lasting weeks to months. The patients rarely present with acute attacks of pain. Jaundice has been reported in up to 70 %–80 % of the patients [2]. In the literature, we have found only few references of acute pancreatitis as a first sign of pancreatic cancer [14, 15].

Pancreatic cancer is the fourth most common cause of cancer mortality in the USA [16]. Chronic pancreatitis, cigarette smoking, obesity, etc. seem to be the known risk factors for pancreatic cancer; only 5–10 % are hereditary in nature. The overall five-year survival rate is 4 %. More than one half of the cases have distant metastasis at diagnosis [17]. Diabetes mellitus (DM) has been lately reported as one of the factors directly linked to the origin of the pancreatic carcinoma but the aetiology connection is not clear [18]. Several studies [19–21] consider DM as a risk factor for pancreatic ductal adenocarcinoma due to a long-lasting disease (either for endocrine involvement, or the common risk factors like obesity, smoking, etc.). However, later studies focused on DM, which rises shortly (2–3 years) before the diagnosis of the tumour as an early symptom [22–25]. This situation seems to be promising for earlier recognition of pancreatic malignancy. It is recommended to examine patients with atypical DM (occurring in older age, with absence of obesity, quick progression to insulin-therapy, etc.) with the most sensitive methods such as endosonography or MRCP to diagnose asymptomatic ductal adenocarcinoma [18].

The explanation of the quick disease progression in our patient is unclear. Little is known about the long-term outcome of AIP and about its malignant potential [26]. The time duration of the disease before the patient was admitted to hospital and the role of corticoids in the progression of the malignancy can be considered.

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PRIMARY SCLEROSING CHOLANGITIS

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ABSTRACT

Primary sclerosing cholangitis (PSC) represents a cholestatic long-waging liver disease, well characterised by inflammation of the bile ducts, which leads to scar formation and narrowing of the ducts over time. The occurrence differs according to geographic conditions. The primary cause of PSC remains unclear. Contemporarily it is supposed to be an autoimmune disease appearing in a field of predisposing gene mutation. The establishment of PSC is based on unique radiological and histological signs in addition to clinical and laboratory signs. The therapy of PSC can be classified from many points of view: specific therapy, the therapy of the complications, pharmacological therapy, endoscope, and surgery. Specific therapy is focused on preventing the progression of the disease. The patients with PSC make up 10 % of all transplantation candidates [7]. The results of this type of treatment are really successful, 85 % of the patients outlast more than one year. Cholangitis and cholangiocellular carcinoma are included to be the most feared complication. Cholangiocellular carcinoma develops in 7–13 % of the patients with PSC [8], most frequently after long-lasting cirrhosis and in combination with colitis ulcerosa. The prognosis of this disease is very poor. Median survival has been estimated to be 12 years from diagnosis in symptomatic patients. Patients who are asymptomatic at diagnosis, and the majority of whom will develop progressive disease, have a survival rate greater than 70 % at 16 years after diagnosis.

Definition

Primary sclerosing cholangitis (PSC) represents a cholestatic long-waging liver disease, well characterised by inflammation of the bile ducts, which leads to scar formation and narrowing of the ducts over time. As scarring increases, the ducts become blocked. As a result, bile builds up in the liver and damages liver cells. Eventually, scar tissue can spread throughout the liver, causing cirrhosis and liver failure.

Epidemiology

The occurrence differs according to geographic conditions, oscillating between 8.5 and 13.6 patients/100 000

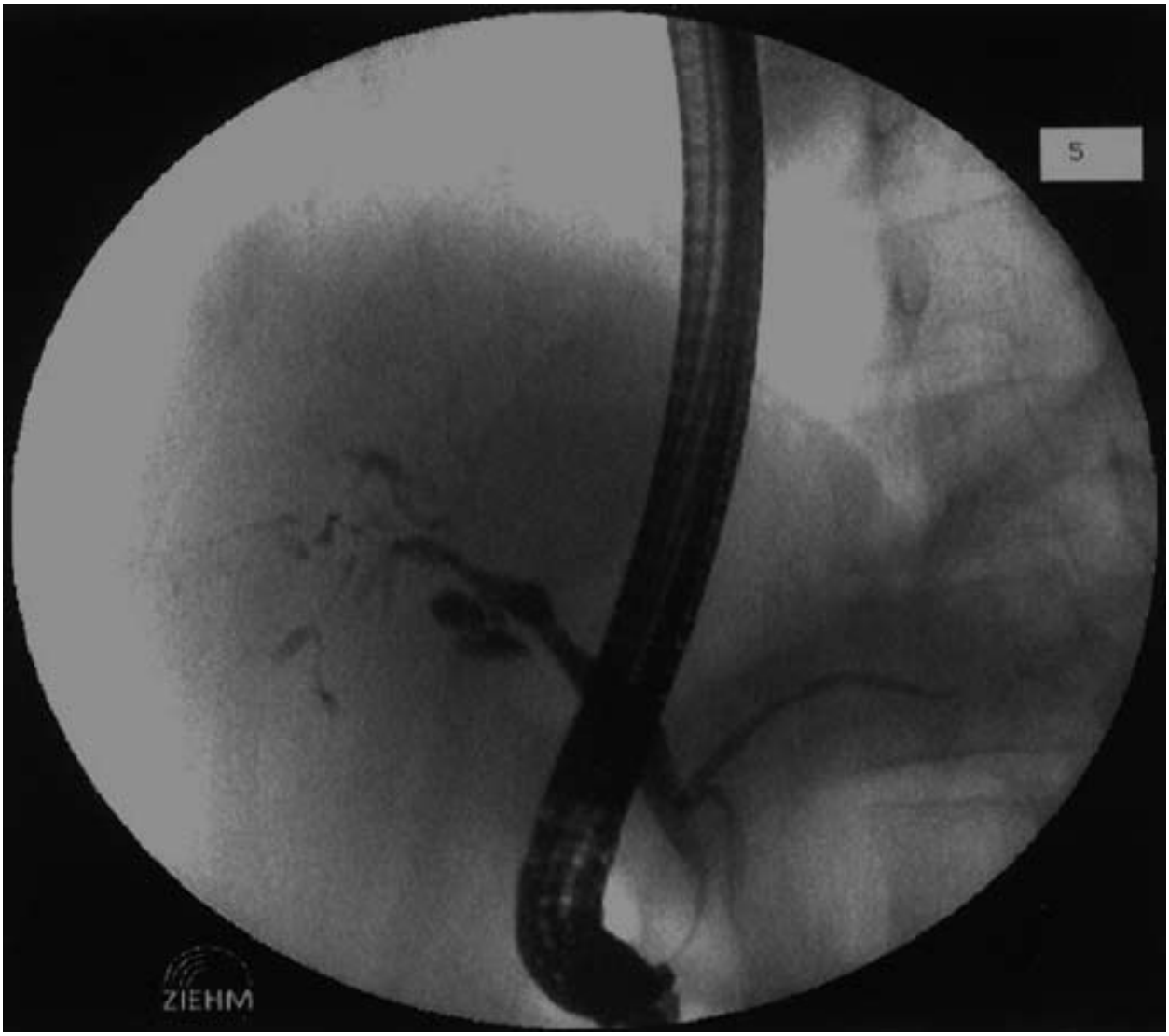

Figure 1
ERCP. Positive findings of alternating areas of stricture and dilated segments of the intrahepatic ducts

inhabitants [1]. The men:women ratio is 2:1. It manifests itself mostly under 40 years of age and the association with other autoimmune diseases is very common, especially with indifferent bowel diseases (IBD). Even in 70 % PSC is related to ulcerative colitis; the association with Crohn's disease is lower [2]. The incidence in the group of patients with IBD remains between 2.4 and 7.5 % [1]. However, no clear dependence has been established between the duration or the activity of IBD and the occurrence of PSC. The patients sustaining extensive bowel damage suffer more from PSC. Despite this fact the bowel inflammation activity is usually low.

Aetiology

The primary cause of PSC remains unclear. Contemporarily it is supposed to be an autoimmune disease appearing in a field of predisposing gene mutation [2]. The starting torqueses are represented by several toxic or infectious agents entering through the large bowel mucosa [3]. In approximately 75 % of PSC patients ANCA (antineutrophil cytoplasm antibodies) is established.

Diagnosis

The establishment of PSC is based on unique radiological and histological signs in addition to clinical and laboratory signs.

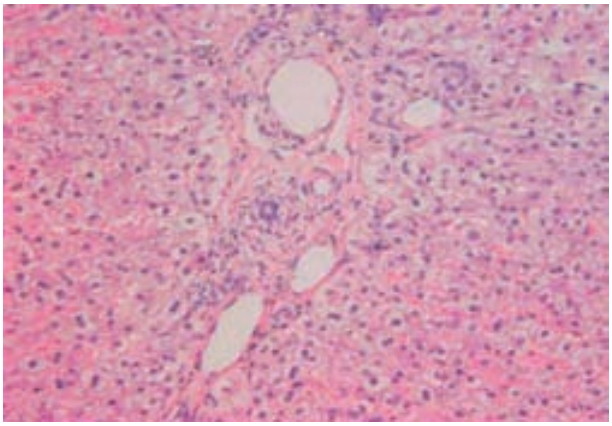

Figure 2
Needle biopsy. Finding of a fibrous enlargement of portal fields

Concerning the clinical signs, most of the patients are asymptomatic at the beginning. The first changes develop after the progression of hepatic malfunction. The patients often complain of tiredness, anorexia, body weight loss, pruritus; later icterus appears. Other clinical signs are connected with hepatic cirrhosis and hepatic failure (ascites, encephalopathy). Laboratory parameters change again in accordance with the clinical course. Anaemia, coagulopathy, and elevation of cholestatic liver enzymes are very common. As already mentioned, ANCA and also ANA, ASMA and anti-ds DNA antibodies are present [3].

Radiological diagnostics

Endoscopic retrograde cholangiopancreatography remains the golden standard in PSC diagnosis. Cholangiopancreatography (ERCP) shows alternating areas of stricture and dilated segments of the intrahepatic ducts characteristic of the "beaded" appearance (Figure 1). However, a non-invasive MRCP seems to be a promising method; its sensitivity achieves 86 %, specificity 77 %, and diagnostic accuracy 88 %. With the use of some specific sequences like a RARE the sensitivity and diagnostic accuracy could increase significantly [4]. According to localisation, we can distinguish three forms of the disease. The first form is classic, afflicting extra and intrahepatic ducts; the second only afflicts intrahepatic ducts, the last form afflicts only big stem ducts [5].

Histological diagnostics

Hepatic biopsy should be part of the diagnostic algorithm, because of its importance in a form afflicting small intrahepatic ducts. In this case radiological findings could be inconclusive. Otherwise, hepatic biopsy could be negative in the case of an extrahepatic form. Therefore, both investigations should be performed together. Furthermore, histological investigation could provide histological staging and finally estimate the prognosis of the patient. Microscopically we can find concentric periductal fibrosis, which can lead to the escape of channels (Figure 2). Therefore, this disease belongs to the vanishing bile duct disease. According to the histological findings we can distinguish four forms of this disease (portal, periportal, septal, and cirrhosis). The typology of the disease is essential for the choice of therapy [6].

The major diagnostic criterion is the finding at cholangiography of irregularly distributed multifocal strictures within both the intrahepatic and extrahepatic bile ducts. The most characteristic histological feature of primary sclerosing cholangitis is periductal concentric obliterative fibrosis of small interlobular bile ducts with or without proliferation of bile ducts in portal tracts, but liver biopsy findings alone are infrequently diagnostic. Nevertheless, liver histology remains important to exclude other causes of chronic cholestasis and for the staging the disease.

Therapy

PSC therapy can be classified from many points of view: specific therapy, the therapy of the complications, pharmacological therapy, endoscope, and surgery. Specific therapy is focused on preventing the progression of the disease. However, presently there does not exist any influential medicamentous treatment that could stop the progression towards cirrhosis. Neither immunosuppressants nor corticosteroids or cyclosporine A, azathioprine or methotrexate have brought any desirable effect. Finally, the use of ursodeoxycholic acid has brought not only the decrease of cholestatic enzymes, but also the improvement of the prognosis (doses of 20mg/kg). Furthermore, we can use antibiotics in the therapy of bacterial cholangitis as a complication of PSC. Important stenoses are solvable by ERCP, with implantation of stents, or with a dilatation. However, final resolution of PSC by means of hepatic transplantation could be difficult because of previous surgeries and endoscopies. The patients with PSC make up 10 % of all transplantation candidates [7]. The results of this type of treatment are really successful, 85 % of the patients outlast more than one year. However, cholangiocarcinoma seems to be an important problem; it develops in between 7 and 13 % of the patients [8]. According to several studies the outcome after the transplantation in patients suffering from cholangiocarcinoma is poor and most of them are dying early succumbing to the recurrence of the disease [9]. Therefore, these patients are excluded primarily from the transplantation programme. Mercifully, in the highly selected minority treatment could be successful with a combination of oncology care and transplantation [10, 11, 12].

Complications

Apart from the above-mentioned cholangitis, cholangiocellular carcinoma is the most feared complication. It develops in 7–13 % of the patients with PSC [8], most frequently in combination with colitis ulcerosa. Early diagnosis is very difficult because of insufficient sensitivity of needle biopsy and brush cytology. According to several studies, a combination of these methods with the detection of the elevation of oncomarkers (CEA, CA 19–9) and imaging methods could be a useful screening method in the detection of CCA in patients suffering from PSC [13, 14].

Most patients with PSC and CCA do not yet have cirrhosis but present with a severe stenosis at the hilum of the liver. The tumour may present as an intrahepatic focal cholangiocellular carcinoma but more often as a ductal infiltrating desmoplastic lesion. Treatment with ursodeoxycholic acid may prevent the development of CCA [15].

The major challenges of CCA in PSC patients relate to a lack of methods for early diagnosis and the absence of effective treatment. Early diagnosis of CCA in PSC is delayed because its clinical presentation can mimic the benign dominant biliary strictures [16]. Moreover, biliary and serum tests to diagnose the development of CCA in PSC are limiting, although the use of advanced cytological techniques for aneuploidy and chromosomal aberrations is promising in this regard [12]. As a result, current therapies do not extend survival with the exception of protocol liver transplantation available to a selected group of patients. Future studies should emphasise the decipherment of the sequence of events transforming the inflammatory changes of the biliary tree to cancer [17]. Only then will chemoprevention, early diagnosis, and therapy of CCA in patients with PSC improve.

Prognosis

The prognosis of this disease is very poor. Median survival has been estimated to be 12 years from diagnosis in symptomatic patients. Patients who are asymptomatic at diagnosis, and the majority of whom will develop progressive disease, have a survival rate greater than 70 % at 16 years after diagnosis [1, 2, 3].

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PSYCHIATRIC ASPECTS OF HEPATIC ENCEPHALOPATHY, HEPATITIS C, AND LIVER TRANSPLANTATION

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ABSTRACT

Psychiatric symptoms often accompany liver disease. The incidence of liver disease has increased recently among psychiatric patients.
Hepatic encephalopathy, defined in broad terms as changes in neurological function resulting from liver disease, encompasses a wide range of neuropsychiatric signs and symptoms that are associated with both chronic and acute liver failure. Hepatic encephalopathy is associated with cognitive dysfunction, impairment of the quality of life, and higher incidence of road accidents.
The incidence of viral hepatitis C has been increasing worldwide. It can cause general slowing of psychomotor performance, disorientation, depression or hypomania, personality disorders, or sleep disorders. Severe depression can be caused by treatment of hepatitis C with interferon alpha. Paroxetine and citalopram show the best proven results in a double-blinded placebo-controlled trials of prophylactic treatment for IFN-α–induced depression.
Before liver transplantation, anxiety, depression and alexithymia are frequent; post-traumatic stress disorder, psychosis and depression (because of survivor guilt) may appear after liver transplantation. In post-transplantation anxiety, women perceive liver transplantation as a psychosocial stressor more than men do. Women also have a worse quality of life after liver transplantation than men.

BACKGROUND

Most liver diseases are associated with neuropsychiatric symptoms and the incidence of liver disease has increased recently among psychiatric patients [1]. The aim of this article is to highlight the most considerable symptoms of selected liver diseases and their treatment. The authors used the Medline database from 1986 to 2009. Recent summary reports as well as original articles were preferred. To search for information, we used the following keywords: "hepatic AND psych*",

"liver AND psych*", "hepatic encephalopathy", "hepatitis C AND psych*", "liver transplantation AND psych*" (searched in Medline, 20.05.2009).

HEPATIC ENCEPHALOPATHY

Hepatic encephalopathy, defined in broad terms as changes in neurological function resulting from liver disease, encompasses a wide range of neuropsychiatric signs and symptoms that are associated with both chronic and acute liver failure [2]. Parts of the clinical picture of hepatic encephalopathy are cognitive function impairment (reduced ability to focus, sustain or shift attention, deficit in both short- and long-term memory, impaired visuospatial performance), incoherent speech, slow and short answers, repetition of words, disorientation, depression or hypomania, apathy or overactivity, anxiety, fear, anger, and personality disorders (jocularity, disinhibition, irritability). Hallucinations (mostly visual) can be present transiently. The patient may have retrograde amnesia for the hepatic encephalopathy episode. Sensitive, but not specific symptoms are sleep disorders such as insomnia, hypersomnia, or inversion of sleep patterns.

As for neurological symptoms, tremor, extrapyramidal rigidity, signs of pyramidal dysfunction, dysarthria, incoordination, impaired handwriting, constructional apraxia, hypoactive reflexes, and ataxia can be present [3].

Encephalopathy reaches 1st–4th grades of clinical state, described in the West Haven Criteria scale [4]. Grade 0, the so-called "subclinical" or "minimal hepatic encephalopathy", could be identified only by neuropsychological or neurophysiological tests [5]. The grades conform to consciousness deterioration, from mild somnolence in grade I and somnolence to stupor in grade III to coma in grade 4 (Table 1). Hepatic encephalopathy is a serious complication of liver disease. Even minimal hepatic encephalopathy is associated with impaired quality of life and higher incidence of road accidents [7].

The mechanisms involved in hepatic encephalopathy still remain to be defined. Insufficient detoxification of neurotoxic substances in the liver is the most important factor in the aetiopathogenesis of hepatic encephalopathy. The development of oedema and swelling of astrocytes because of quick accumulation of nitrogenous substances and changes in cerebral blood flow is typical of encephalopathy in acute liver failure. Chronic encephalopathy has a more complex mechanism of development. There are changes present in the GABAergic and glutamatergic system and increase of peripheral benzodiazepine receptors. Increased serotonin turnover, raising deposition of manganese in basal ganglia, specific changes in blood-brain barrier permeability, formation of false neurotransmitters from nitrogenous substances which compete with dopamine and norepinephrine, and many other factors are present in the brain of a patient with hepatic encephalopathy [8]. TIPS (transjugular intrahepatic portosystemic shunt) makes a shunt circulation which bypasses the liver. Due to this circulation, the brain is damaged by toxic substances causing hepatic encephalopathy, which has mostly the character of chronic or episodic encephalopathy.

Hepatic encephalopathy is treated with the non-absorbable disaccharide lactulose (10–30 ml p. o. à 8 hours) [9]. It reduces the intestinal production/absorption of ammonia because of its laxative effect, increased incorporation of ammonia into the proteins by colonic bacteria, and interference with uptake of glutamine by intestinal wall [10]. Hepatic encephalopathy can be also treated with rifaximine 400 mg à 8 hours [11]. Neomycin 1–3 g p. o. à 6 hours was approved by the FDA (Food and Drug Administration) in the treatment of acute hepatic encephalopathy [12], but this drug is not available in the Czech Republic. The beneficial effects of both rifaximine and neomycin relate to their ability to eliminate urease-producing organisms from the intestinal tract [9]. L-ornithine-L-aspartate (6 g p. o. or in infusion three times a day) [13] or infusion with branched amino acids can support the treatment effect. The benefit of branched amino acids might stem from increased liver regeneration; L-ornithine-L-aspartate has been shown to reduce circulating ammonia levels [10]. Albumin dialysis MARS (Molecular Adsorbent Recirculating System) can also improve hepatic encephalopathy [14].

The off-label indication is benzodiazepine antagonists (flumazenil 0.2 mg slowly i.v., max. 1 mg p. d.), which have short-time duration but great effect [15]. Sodium benzoate binds the ammonium cation, which is then excreted as hippurate into the urine. It can be used as off-label indication, 5 g two times a day [16]. Probiotics seem to be a suitable supplement of the therapy [12]. Manganese chelation and N-methyl d-aspartate (NMDA) antagonists have recently been tested in laboratories [12].

HEPATITIS C

The prevalence of viral hepatitis C goes up worldwide as well as in the Czech Republic (Figure 1). It has become the most common indication for orthotopic liver transplantation in most Western countries [18]. Infected lymphocytes can cross the blood–brain barrier. After that, the virus starts to replicate in the central nervous system, and neurotoxic cytokines are released from infected cells [1, 19].

In people with hepatitis C, cognitive dysfunction, mostly attention deficit, and working memory deficit are often present [20]. People infected by hepatitis C frequently have mild depression. The rate of depression is associated with the inflammation activity [21]. Patients with hepatitis C are often drug and alcohol abusers. Interferon therapy is expensive, and

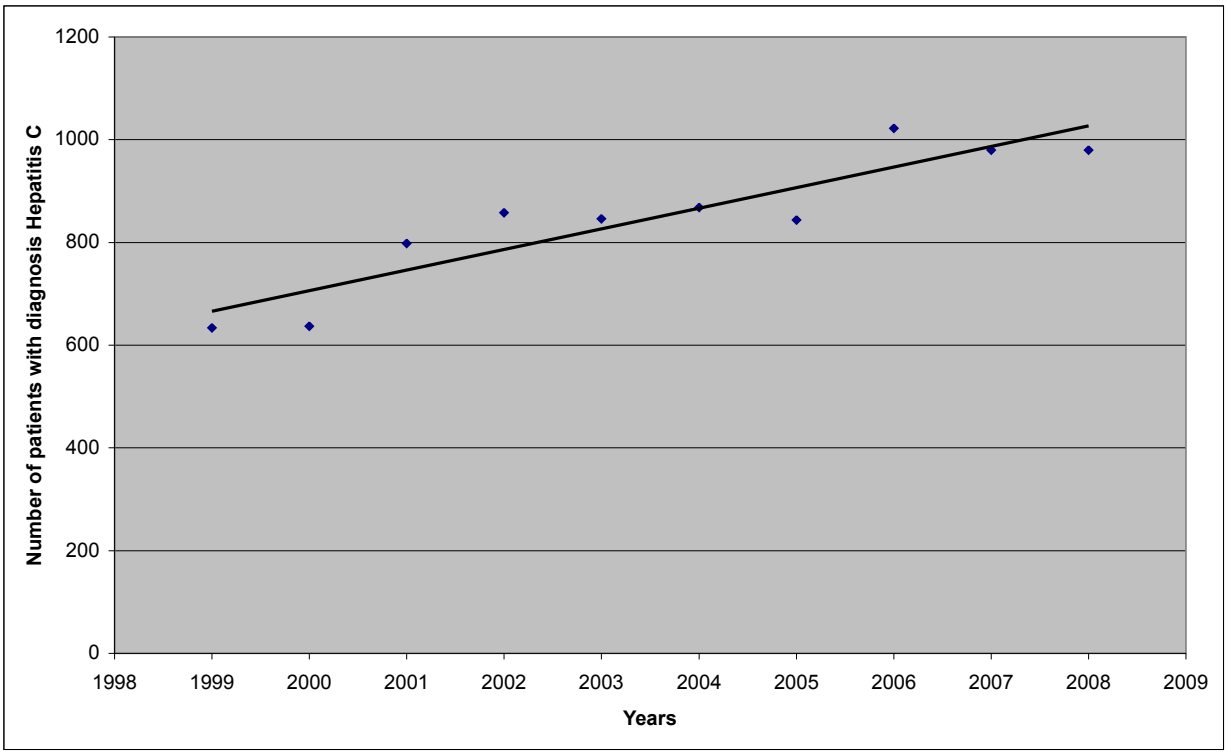

Figure 1
The prevalence of hepatitis C in the Czech Republic
Comment: Coefficient of determination 0.84. Source: SZÚ, 2009

before we start with the therapy, the patient should abstain from addictive substances. We know that abuse of alcohol during interferon alpha treatment is associated with diminished treatment response [22].

The interferon therapy has neuropsychiatric side effects, including cognitive impairment, apathy, and medium-serious to serious depression [23]. Nowadays still more authors have been recommending to give antidepressants preventively during INF-alpha treatment [1, 24]. Paroxetine and citalopram show the best proven results, in a double-blinded, placebo-controlled trials of prophylactic treatment for IFN-α–induced depression [25, 26]. A good result was found with the use of fluoxetine and sertraline [27, 28, 29]. If the patient is nicotine dependent, bupropion could be a suitable choice. Bupropion has also the potential to improve cognitive impairment and psychomotor retardation associated with IFN-α therapy [1, 30]. In case that the patient has marked psychomotoric retardation and no history of abuse, psychostimulants can help to manage fatigue, apathy, and cognitive slowing (modafinil 200 mg p. d.) [1]. Atypical antipsychotics are more suitable than mood stabilisers in the management of psychotic, manic, or hypomanic symptoms [31, 32, 33].

Administration of ribavirin is associated with a higher incidence of insomnia and depression [34]. The treatment of these side effects is similar to the management of IFN-related neuropsychiatric adverse effects.

LIVER TRANSPLANTATION

Before liver transplantation, anxiety, depression and alexithymia are frequent mental problems [35]. Trzepacz et al. [36] determined a psychiatric diagnosis in half of 247 liver transplantation candidates (adjustment disorder being the most frequent). In the Czech Republic, abstinence from drugs and alcohol for at least six months is a requirement for patients to be included in the waiting list [37], so some of them require psychiatric treatment for drug dependency. The patient's adherence is also one of the criteria. Liver diseases often cause depression. Depression induces apathy, which is associated with reduced compliance. That is why the treatment of depression is so important when we consider liver transplantation [38].

Table 1
West Haven Criteria

West Haven Criteria	
Grade	Symptoms
I	Mild confusional state
	Euphoria, anxiety, irritability or depression
	Attention deficit
	Slowing in psychomotor performance
	Sleep disorders
II	Hypersomnia
	Lethargy
	Personality changes
	Transient disorientation in time and place
III	Somnolence to stupor
	Pronounced disorientation
	Severe memory deficit (retrograde amnesia)
	Unintelligible speech
IV	Coma with (IVa) and without (IVb) the reaction to painful stimulus

Comment: Sources: Conn 1993, Sherlock 2002

An interesting topic is the psychodynamic aspect of liver transplantation: patients often identify themselves with donors. They give names to the new organ and try to imagine the donor's appearance and what their personal characteristics are like. Sometimes they fear that when a living donor dies they will also die. Storkebaum [39] described one of her patients: she was a lesbian, who rejected the transplantation because she was scared that she might receive a man's liver. In 1973 Basch already described his experiences with patients who had stopped taking their antirejection medication and died, after they had knowledge of the donor and felt repulsion for him or her [40].

After transplantation, anxiety, post traumatic stress disorder, psychotic symptoms and depression may appear [35]. Women especially feel unattractive after the transplantation and are afraid whether the partner will accept their 'new body' [39]. Women perceive more psychosocial stress with liver transplantation than men do; women also have a worse quality of life after liver transplantation than men [41].

Post-transplantation depression can be interpreted as the reaction to the loss of their own organ, which can feel similar to the loss of a family member. It also can be a reaction to the experience of total helplessness and dependence on the doctors' care [39]. Post-transplantation depression can be associated with the survivor guilt: 'Somebody had to die, so that I can now live'. Psychic problems are often present in people who had the experience of their relative dying after or during major surgery. They can feel guilty because they did not die (Why do I live, when he/she did not?). This so-called 'survivor guilt' was described in the Vietnamese war: soldiers had depression and felt guilty when their friends died but they were alive [42]. In preliminary discussions, a psychiatrist or psychologist anticipates these complications, and offers counselling to reduce psychological problems.

An important problem is the prevention of the relapse of alcohol abuse after liver transplantation. Gedaly et al. [43] described relapse in 19 % of 387 patients with alcohol abuse history.

CONCLUSION

Patients in the care of hepatologists could profit from a close co-operation between psychiatrists and internal specialists,

because lots of patients suffer from psychiatric comorbidity. In the Czech Republic, we do not have any consultation – liaison psychiatry as an independent specialisation. The problems of patients hospitalised at somatic wards differ from the care in psychiatric clinics, so this subspecialisation is needed. In more developed countries, this subspecialisation is a common part of psychiatry and we should start to consider this as well.

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INTESTINAL MICROFLORA AND BACTERIAL TRANSLOCATION

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ABSTRACT

This article presents an overview of the development of the intestinal microflora, its composition and function in individual parts of the gastrointestinal tract, and the role of both internal and external factors. The impact of the intestinal microflora on the immune system is explained as well as potential effects of antibiotics including selective decontamination. Special attention is paid to intestinal overgrowth of bacteria, which may even lead to their translocation into the extraintestinal sites. Besides bacterial factors, unwanted overgrowth is facilitated by the intestinal mucosal and immune systems.

The intestine of men is a tube about 10 metres long and its extremely irregular surface is covered with a single layer of epithelial cells, representing an area of approximately 200 m^2. The intestine is sterile during foetal development and is first colonised only as the foetus passes through the birth canal. The gut is rapidly colonised after the birth by many microorganisms whose composition varies markedly in the first days of life. Breastfed babies are earlier colonised by those bacterial genera typical of the intestinal microflora of adult humans [1] and e.g. bifidobacteria are less frequent in those who are formula-fed. Preterm infants, babies born by Caesarean section and those hospitalised for a long time have an aberrant composition of the intestinal microflora. Their normal healthy microflora, comprising mainly lactobacilli and bifidobacteria, is replaced by hospital strains, such as potentially pathogenic enterococci, staphylococci, enterobacteria, and others. Major changes in the character of the intestinal ecosystem occur after the baby is no longer breastfed, but the initial intestinal colonisation is crucial for the further development of humans as the present bacteria may modulate gene expression in epithelial cells and thus produce a favourable environment for themselves [2].
The intestinal microflora weighs over 1 kg and contains an enormous number of microbes – their amount is more than ten times the number of cells in the human body. The intestinal microbial community comprises over 500 species, of

Table 1
Composition of the human gastrointestinal tract (from Nord and Kager, 1984)

Microorganisms	**Numbers of microorganisms (CFU/1 ml or CFU/1 g)**			
	stomach	jejunum	ileum	colon
Total bacterial count	$0–10^3$	$0–10^5$	$10^3–10^9$	$10^{10}–10^{12}$
Aerobically growing agents				
Family *Enterobacteriaceae*	$0–10^2$	$0–10^3$	$10^2–10^7$	$10^4–10^{10}$
Streptococci	$0–10^3$	$0–10^4$	$10^2–10^6$	$10^5–10^{10}$
Staphylococci	$0–10^2$	$0–10^3$	$10^2–10^5$	$10^4–10^9$
Lactobacilli	$0–10^3$	$0–10^4$	$10^2–10^3$	$10^6–10^{10}$
Yeasts	$0–10^3$	$0–10^2$	$10^2–10^4$	$10^4–10^6$
Anaerobic bacteria				
Bacteroides	rare	$0–10^3$	$10^3–10^7$	$10^{10}–10^{12}$
Bifidobacteria	rare	$0–10^4$	$10^3–10^9$	$10^4–10^{11}$
Peptostreptococci	rare	$0–10^3$	$10^2–10^6$	$10^{10}–10^{12}$
Clostridia	rare	rare	$10^2–10^4$	$10^6–10^{11}$
Eubacteria	rare	rare	rare	$10^{10}–10^{12}$

which most have never been cultured and many have not even been identified, and contains both autochthonous or resident bacteria and allochthonous or transient bacteria, i.e. those only passing through the intestine [3]. The relationship between the host and the bacteria in the intestinal microflora also plays an important role in postnatal development, intestinal maturation, and development of the mucosal immune system [4].

1. MICROFLORA IN THE INDIVIDUAL PARTS OF THE GIT

The normal microflora is an enormously complex ecosystem comprising both aerobic and anaerobic microorganisms. Together with the mucosal immune system, it protects the host's organism from pathogen invasion and plays a positive role in certain metabolic processes [5].

In the oral cavity, anaerobes predominate over aerobes in a ratio of about 100:1. Together with saliva and food, oral microorganisms pass through the oesophagus to the stomach. In the oesophagus, the analogical microflora multiplies, especially under pathological conditions, such as in the case of any oesophageal obstruction, both organic and functional. Other contributing factors include severe devastating conditions and immune insufficiency. In such cases, candida or viral infections are involved, e.g. in candida or viral oesophagitis.

Most microorganisms passing from the oral cavity to the stomach are destroyed by acid gastric juices. Thus, the stomach of healthy individuals is usually sterile, with the transient microflora being mostly gram-positive and aerobic. The concentration of microorganisms is usually less than 10^3 CFU/1 ml. The most commonly isolated genera are enterococci, staphylococci, lactobacilli, and yeasts.

The microbial flora of the oral part of the small intestine has a composition similar to that of the stomach and is influenced to a certain extent by pathological conditions of the stomach. In patients with duodenal ulcers or even bleeding ulcers, pyloric obstruction or cancer of stomach, a mixture of aerobes and anaerobes is found. Achlorhydria and bacterial overgrowth are also connected with drugs reducing gastric acidity, e.g. H_2 blockers and proton pump inhibitors (PPI). The normal concentration of bacteria is $10^{3–4}$ CFU/1 ml. Enterobacteria are sometimes present in a concentration of 10^{2-5} CFU/1 ml. Microbes increase in number especially in intestinal stasis (intestinal obstruction, blind loop syndrome). In the jejunum, aerobic and gram-positive bacteria prevail. However, coliform and anaerobic bacteria are also present there, even more commonly than in the stomach. In the distal ileum, gram-negative microorganisms begin to predominate over gram-positive bacteria. The similarity to the large intestinal microflora is due to microorganisms penetrating through the ileocaecal valve (backwash mechanism).

The numbers of aerobic and anaerobic microorganisms increase with the distance from the ileocaecal valve. Live bacteria account for about one third of faecal dry matter. The prevailing aerobe is *Escherichia coli*, which may be isolated in a concentration of $10^{7–8}$ CFU/1 g of stools. Anaerobes are dominated by *Bacteroides fragilis* and *Eubacterium* spp. Also frequent are anaerobic gram-positive cocci (*Peptostreptococcus* spp., *Peptococcus* spp., *Clostridium* spp.). Additionally, aerobically growing enterococci and various members of the *Enterobacteriaceae* family are commonly isolated. In the colon, bacteria significantly increase in number orally from an obstruction of any origin.

2. FACTORS INFLUENCING COMPOSITION OF THE INTESTINAL MICROFLORA

The composition of the intestinal microflora is mostly regulated by saliva (antibacterial activity of lysozyme, lactoferrin and rhodanide), gastric acid (pH) and pepsin, bile containing bile salts and unconjugated bile acids, pancreatic juice (lipase), intestinal motility, and regeneration of intestinal mucosal cells. The microflora has its own regulatory mechanisms (colonisation resistance) that prevent penetration of unwanted organisms and substances and inhibit pathogenic microflora by bactericidal action of short-chain fatty acids and production of hydrogen peroxide or hydrogen sulphide. Important are cellular (intestinal lymphoid tissue, T and B lymphocytes) and humoral (secretory immunoglobulin A) immune defence mechanisms [6].

The intestinal system could be severely affected by ageing and some diseases and their treatment – reduced salivary secretion in Sjögren's syndrome, long-course radiotherapy of the head and neck, after surgery (gastrectomy, vagotomy), biliary obstruction, pancreatic insufficiency, treatment with H_2 blockers, proton pump inhibitors, prokinetics, laxatives. Under such circumstances, coliform and potentially pathogenic bacteria grow in number and the risk of salmonella, shigella or candida infection increases.

The external factors influencing the composition of the intestinal microflora include nutrition, treatment, environment, and stress.

3. FUNCTIONS OF THE NORMAL MICROFLORA

The intestinal microflora has many important functions: to maintain a microbial barrier against obligate and potential pathogens, to stimulate the intestinal immune system and thus the so-called common mucosal immune system, to reduce bacterial translocation, to affect motility and perfusion of the intestinal wall, and to produce vitamins.

The gradual transition from aerobes dominating the upper intestine to anaerobes predominant in the distal portions represents the basic functional and structural changes. In the entire microsystem, aerobes are responsible for the so-called scavenging effect. It means that they, in particular *Escherichia coli*, consume oxygen in oxidative phosphorylation reactions in energy metabolism. Distally, the redox potential decreases, facilitating the growth of anaerobes, otherwise sensitive to the presence of oxygen due to their enzyme make-up (catalase, cytochrome oxidase, superoxide dismutase) insufficient to eliminate superoxide and other oxygen radicals. Thus, the existence of the two groups of microbes is mutually determined as any damage to aerobes apparently leads to subsequent harm to the anaerobic population [7,8]. Impairment of the microsystem of the original intestinal microflora is common in patients with chronic liver disease. Significantly increased numbers of live aerobic gram-positive and gram-negative bacterial species are repeatedly found in the faeces of cirrhotic patients [9].

4. COLONISATION RESISTANCE

Colonisation resistance of the gastrointestinal tract is the microbial barrier made of beneficial commensal bacteria in the intestine and preventing pathogens from overgrowing. It acts against both obligate (salmonella, shigella, yersinia, campylobacter, vibrio, and other species) and potential pathogens (clostridia, candidas, etc.) [10]. It also controls the opportunistic microflora (enterobacteria, pseudomonas, staphylococci, streptococci, etc.).

Colonisation resistance is based on growth inhibition and/or killing of foreign microorganisms, competition for substances, vitamins and growth factors, lowering intestinal pH, and direct antagonism of the normal microflora against the obligate and potentially pathogenic microflora [11].

5. THE INTESTINE AND THE IMMUNE SYSTEM

The present commensal intestinal microflora activates antiinflammatory intestinal systems protecting the intestinal epithelium from inflammation as a reaction to invading pathogens [12], but the intestinal commensals have also a huge regulatory effect on immune responses even outside the intestinal tract [13]. The human organism has mechanical, chemical and immunological barriers which, at the point of contact, protect its internal environment from uncontrolled penetration of antigenic and mitogenic stimuli. The main barriers and contact places involve mucosal surfaces of the digestive, respiratory and genitourinary tracts. The intestinal mucosal immune system provides a barrier against pathogenic microorganisms and immunogens from the diet. The basic features of the mucosal immune system are prevailing IgA antibodies, preferential colonisation of both mucosae and excretory glands by cells originating from intestinal lymph follicles and, finally, polymeric immunoglobulins transported to the secretion through epithelial cells.

The gut-associated lymphoid tissue (GALT) is a system that processes information from about 100–200 tons of food per lifetime and is permanently colonised by the normal and, intermittently, non-physiological microflora. The GALT develops mainly in the early postnatal period and is made up of organised lymphoid tissue, free intraepithelial lymphocytes, and lamina propria lymphocytes.

The immune reaction in the GIT mucosa produces not only local but also general immune response in other mucosae or

distant organs, the so-called common mucosal immune system. Following their contact with allergens, cells, especially those in the intestinal mucosa, migrate to regional lymph tissue (Peyer's patches, lymph nodes), via the lymphatic system to the bloodstream and from there to all mucosae and endocrine glands (the so-called homing).

6. BACTERIAL TRANSLOCATION

The microflora of GIT is continuously affected by many physical, chemical and biological factors. Therefore, it is a constant potential source of diseases of the GIT or the entire organism. Changes may occur in the total number, localisation, representation of genera or species, and in the metabolic activity of microorganisms.

The term bacterial translocation was first used in 1979 [14]. Bacterial translocation is defined as either active or passive penetration of living microorganisms and their toxic products through the mucosal epithelial layer to the lamina propria mucosae. From there, microbes migrate to mesenteric lymph nodes and/or extraintestinal sites [14]. Under normal circumstances, these are only small numbers of bacteria readily destroyed by the immune system in the lamina propria mucosae. Translocation is only possible if their numbers are high, up to 10^8 bacteria in 1 gram of faeces, as reported in the literature [15,16].

According to the clinical significance, there are four degrees of bacterial translocation [17,18]:

Degree 0: bacteria and/or their components penetrate the mucosa by various mechanisms: active intracellular penetration, diffusion, absorption, endocytosis, or phagocyted by macrophages.

Degree 1: bacteria and/or their components enter the mesenteric lymphatic system and penetrate it centripetally.

Degree 2: bacteria and/or their components are already detectable in the systemic circulation and certain organs. They may also pass directly into small intestinal venules and from there into the portal circulation. Part of the bacteria are probably even capable of intracellular passage through the muscularis propria into the peritoneal cavity (this was the reason for adjusting the original 1985 Berg's definition according to which bacterial translocation is a passage of bacteria and/or their components from the intestinal lumen into the lymphatic system with potential systemic penetration into various organs).

Degree 3: the organism is systemically overwhelmed by bacteria and/or their components, leading to the septic response.

The main mechanisms underlying the translocation are deficient local mucosal immune response, lower phagocytic activity of both macrophages and neutrophils, increased permeability of the intestinal barrier, and the above-mentioned intestinal bacterial overgrowth [15,19]. Bacteria escaping both phagocytosis and destruction by the complement system may even get into the bloodstream. Considering bacteria commonly found in the gastrointestinal tract, only some of them participate frequently in the translocation. The most frequent bacteria are *Escherichia coli*, *Proteus* spp., *Klebsiella pneumoniae*, and other *Enterobacteriaceae*, *Pseudomonas aeruginosa*, enterococci, streptococci, and staphylococci – i.e., those causing infections in immunocompromised individuals. Bacterial small-intestinal overgrowth creates conditions favourable for the translocation of the above mentioned bacteria.

The factors influencing bacterial translocation may be divided into three groups: bacterial factors, factors of the intestinal wall, and defensive factors (local or systemic).

Bacterial factors

The presence of commensal microflora is very important for all defence mechanisms [20]. The biological pressure of intestinal microbes is essential for maintaining the mucosal barrier function [21]. Impaired physiological microbial balance (e.g. in acute pancreatitis, liver cirrhosis, or due to morphine administration) results in dysfunction of the mucosal barrier and increased bacterial translocation. Thus, potential pathogens penetrate outside of the intestine. If obligate anaerobic intestinal bacteria outnumber the aerobically growing species by more than 100 to 1, translocation is exceptional [22].

Intestinal mucosal barrier factors

The primary function of the intestinal mucosal barrier is to maintain the host's integrity by monitoring the contents of the intestinal lumen and protection against invading bacteria and their toxins [20]. Thus, intestinal epithelial cells form an important physical barrier between the intestinal lumen and the human internal environment. Their tight arrangement and fluid secretion represent non-specific protection from bacterial translocation. The function of epithelial cells is supported by other defensive products such as mucus and defensins (small peptides containing cysteine, with high antimicrobial activity).

The immune system

Specific protection against the present antigens is maintained by continuous monitoring of the intestinal contents by the intestinal immune system (GALT) able to distinguish between invasive microorganisms and harmless antigens such as dietary proteins or commensal microorganisms. The primary immunological barrier is a layer of intestinal epithelial cells. In addition to their non-specific barrier function, they are capable of recognising preserved microbial structures by the so-called Toll-like receptors (TLRs). When these are activated by cell-wall lipopolysaccharides of gram-negative bacteria or

by lipoteichoic acid of gram-positive pathogens, a process resulting in the inflammatory defence response is initiated [23]. If bacteria break the mucosal line of enterocytes, they encounter macrophages and dendritic cells, currently intensively investigated for their essential role in intestinal immunology. Their task is to monitor the intestinal contents. Their long processes reach the intestinal lumen, passing among tightly connected epithelial cells without breaking the mucosal barrier. The dendrites sample the present bacteria and other antigens and present them to the GALT. This is how continuous communication between the intestinal bacteria and the GALT is maintained [24].

The well-balanced gastrointestinal microflora, together with intact structural and immunological barriers, plays an essential role in preventing infectious complications. Therefore, prevention of bacterial overgrowth, promotion of intestinal barriers and modulation of the immune response are promising for prophylactic care and prevention of both early and late infectious complications in severely ill patients.

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OBSTIPATION AND DIARRHOEA – A COMMON AND SIGNIFICANT PROBLEM IN THE ELDERLY

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ABSTRACT

Constipation and diarrhoea are common complaints in older people, and many people become gradually more constipated with age. Lack of symptoms is typical of the disease in the elderly. If we are unable to properly evaluate abnormal manifestation and atypical connection and to assign them to the right diagnosis, the consequences can be serious.
Constipation is a common complaint in older people, and many people become gradually more constipated with age. Prevention and change in dietary habits are important. Adding fibre and sufficient hydration are helpful. Only then we can use laxatives, especially osmotic or bulk-forming ones.
Diarrhoea is a common problem in elderly persons. Worldwide, diarrhoea is the second leading cause of mortality. In the developed world, 85 % of its mortality affects the elderly. The main causes of diarrhoea include drugs, thyrotoxicosis, diabetes mellitus, microscopic colitis, diverticulitis, and mesenteric ischaemia. Very important is diarrhoea caused by Clostridium difficile as a result of antibiotic treatment. Rehydration must be maintained to prevent hypotension and organ failure in the often multimorbid patient.
False diarrhoea develops in case of faecal impaction and is connected with the development of faecaloma. It is particularly concentrated in the institutionalised or impaired elderly. The clinical consequences may be disabling and occasionally life-threatening.

INTRODUCTION

Constipation and diarrhoea in the elderly is a common problem. The causes of those conditions are little different from the causes in young age, so we are trying to describe the specifics of those problems in the elderly. Lack of symptoms is typical of the disease in the elderly. If we are unable to properly evaluate abnormal manifestation and atypical connection and to assign them to the right diagnosis, the

consequences can be much more serious, because the geriatric patient has substantially lower reserves and adaptation mechanisms than the young one. Let us take a closer look at those conditions.

DISCUSSION

Constipation

There is no doubt that constipation appears much more often in older people than in young ones. Constipation is a common complaint in older people, and many people become gradually more constipated with age [1, 2]. Constipation has a significant subjective component, so we must first make clear what the patient means by their constipation complaints. Usually it is less frequent and/or difficult defecation of stools in comparison with the past. Which defecation frequency is normal differs from patient to patient – it varies from once in 3 days to 3 times a day.

Pathophysiology: motility problems (inert colon), excessive water absorption (diuretics in medication) or problems with defecation mechanics in the terminal part of the gastrointestinal tract (anorectal outlet obstruction). Motility problems in the elderly can be caused by drugs which are used for another reason (see Table 1).

Table 1
Drugs causing constipation

Calcium blockers
Codeine and its derivatives
Drugs containing calcium
Morphine and other opiates
Diuretics
Antacids containing aluminium

Problems with defecation mechanics contain rectal intussusception, prolapsed rectum, and asynergy of pelvic floor muscles. It is important to ask elder women about difficulties during the births, because this can be the initiation factor of defecation problems [1].

Constipation can be organic (inflammatory strictures, tumours), secondary (hypothyroidism, diabetes mellitus, drugs), or it can be a specific disease, the so-called functional constipation.

Constipation has a significant psychological impact on the afflicted person. It negatively influences their mood and causes depression. Improper usage of laxatives causes a sense of insecurity and limits social activities.

Diagnostics: very important is the patient's history. Constipation usually lasts longer and valuable information can be acquired by asking the patient why they decided to attend the doctor (e.g. pain during defecation, rectal bleeding). Pharmacological history is essential as well. During the examination we are searching for other diseases (hypothyroidism). Repeated clinical controls of the patients are necessary to monitor the evolution of the clinical conditions. Do not forget per-rectum examination: some colorectal carcinomas are within the reach of the inspecting finger. We can also measure the transit time of X-ray contrast marks through the gastrointestinal tract. Defecography is best for the evaluation of defecation mechanics problems.

Therapy: we must inform the patient in an intelligible way about the physiology of defecation. We must explain to the patient that there is no need of daily defecation. An organism with intact bowels cannot be intoxicated by bowel content.

Dietary habits are also important. At first we add sufficient amount of fibre. We usually choose simple natural agents (dried plums, fruit, vegetables). We must take heed of proper hydration (at least 2 litres of fluids per day). If adding fibre is not enough, we add additional fibre in the form of wheat bran (just mix several spoonfuls with yoghurt and drink a lot). If it is possible, increased physical activity is also helpful. The underlying mechanisms regarding the association between physical exercise and constipation are unclear but a favourable effect on colonic motility, decreased blood flow to the gut, biomechanical bouncing of the gut during running, compression of the colon by abdominal musculature, and increased fibre intake as the result of increased energy expenditure have all been reported. The Nurses' Health Study, which followed a cohort of 62,036 women, found that physical activity 2–6 times per week was associated with a 35 per cent lower risk of constipation [3]. Take a look at the patient's medication as well, to check if all drugs used are necessary.

Laxatives are usually unavoidable. However, long-term usage of stimulating laxatives is inappropriate. We can use bulk-forming or osmotic laxatives (psyllium, methylcellulose, polyethylene glycol, magnesium salts, lactulose), or glycerine suppositories. Bulk-forming laxatives (psyllium, wheat bran) are not suitable in case of defecation mechanics problems. Osmotic laxatives are more suitable in those cases. Osmotic laxatives soften the stools and by this way augment defecation.

Prevention and therapy of the so-called faecaloma are very difficult. It means stagnated stool in the rectum, especially in cachectic immobilised old people. There can even be false diarrhoea with stool incontinence (see below). We can try oil enema or enema with polyethylene glycol [4]. Sometimes stools can be removed from the rectum only via manual extraction.

Diarrhoea

There are similar causes of diarrhoea in the elderly as in younger age. We keep our eyes on the causes appearing in the elderly. Diarrhoea is a common problem in elderly persons. Worldwide, diarrhoea is the second leading cause of mortality. In the developed world, 85 % of its mortality affects the elderly [5].

In case of acute diarrhoea (up to two weeks) we consider infection, especially in patients living in the community (retirement homes, hospitalised patients). If diarrhoea persists for more than 24 hours, oral rehydration solutions or intravenous fluids must be administered promptly in order to prevent hypotension and organ failure in the often multimorbid patient. Other common factors causing diarrhoea are acute alimentary indigestion and drugs.

In case of chronic diarrhoea, there are several common causes in older age (see Table 2).

Table 2
Causes of diarrhoea in the elderly

Drugs
Thyrotoxicosis
Diabetes mellitus
Systemic sclerosis
Microscopic colitis
Mesenteric ischaemia
Diverticulitis
Colorectal carcinoma

Drugs as a cause of diarrhoea

Diarrhoea can be a simple adverse effect of a given drug. In the rapidly increasing elderly population, diarrhoea as the result of drug therapy is an important consideration. The elderly consume a disproportionately large number of drugs for multiple acute and chronic diseases. Drugs can compromise both immune and non-immune responses. Ageing decreases the quality and proportion of T cells, which in turn reduces the production of secretory IgA, the primary immune response of the gut. Acid production in the stomach decreases with increasing age and this compromises its vital 'self-sterilising' function, thus increasing the risk of diarrhoea due to viral, bacterial, and protozoal pathogens. Other non-immune defence mechanisms include the motility of the small intestine and the host-protective commensal bacteria of the colon. Drug-induced hypomotility may result in bacterial overgrowth, deconjugation of bile salts, and diarrhoea. Less commonly, diarrhoea may occur due to hypermotility because of a cholinergic-like syndrome. In the colon the host-protective commensal bacteria provide a powerful defence against pathogens [6].

Treatment with broad-spectrum antibiotics can often result in diarrhoea caused by the toxin of *Clostridium difficile*. Many studies describe that this complication afflicts especially old, frail and weakened patients [7]. The symptoms of this serious iatrogenic complication vary in a wide spectrum – from light diarrhoea to fulminant colitis, which threatens the patient's life. Pseudomembranes are a typical finding during endoscopy, but in many times they are missing [7]. A proof of the *Clostridium difficile* toxin in the stools is the most important part in the diagnostics of this condition. To treat it we can use metronidazole or vancomycin. What is advised is reasonable administration of antibiotics and trying to avoid broad-spectrum antibiotics if possible. In one study Ludlam found that reducing the patient's exposure to injectable third-generation cephalosporins by substituting alternative antibiotics can produce a cost-effective reduction in the incidence of antibiotic-associated diarrhoea [8]. Sometimes, diarrhoea can be caused by fungal overgrowth after antibiotic therapy [9]. Drugs causing diarrhoea are summarised in the following table (see Table 3).

Table 3
Drugs causing diarrhoea

Antibiotics	Bile acids
Theophylline	NSAIDs
Antacids with magnesium salts	Colchicine
Laxatives	Cytostatics
Antisecretory drugs (rare)	Hymecromone
Statins and fibrates	Radiation

Though the causes of diarrhoea are diverse, a drug-associated aetiology should always be considered and actively sought and addressed to prevent the complications of dehydration, electrolyte imbalance, and undernutrition.

Diseases as a cause of diarrhoea

Diabetes mellitus is a frequent cause of diarrhoea in older people. Diarrhoea can afflict patients with type 2 diabetes as well as those with type 1 diabetes. The main symptom is diarrhoea of varying intensity, usually after meals and even during the night. Especially night diarrhoea can end in stool incontinence. There can be present other symptoms of neuropathy (orthostatic hypotension, night sweat, paraesthesia, problems with urination). The cause of chronic diarrhoea in diabetics is vegetative neuropathy of nerve plexuses in the gastrointestinal tract. In some cases diarrhoea is caused by dysmicrobia. If we succeed in cholestyramine therapy, we can assume malabsorption of bile acids. Quite commonly, a test of several therapeutic approaches is done to find the most suitable one.

Hyperthyroidism in the elderly can have only few symptoms; dominating are muscular weakness, weight loss, and diarrhoea.

Other causes are similar to those in younger age. Older people are much more threatened by dehydration, electrolyte disruption and nutritional deficit, because the reserves and adaptation mechanisms of older patients are substantially lesser than in young ones.

Non-specific inflammatory bowel diseases

This category includes ulcerative colitis and Crohn's disease. They both have bimodal age distribution. The first peak appears in adolescents and young adults, the second peak appears between 50–80 years of age. In 15% of the patients colitis develops after 65th year of age [7]. Older people are not protected against chronic bowel inflammations. Typical characteristics are similar to the common picture of the disease. The main symptom is diarrhoea, usually with bleeding.

Microscopic colitis (collagenous and lymphocyte) can cause diagnostic problems, because the macroscopic endoscopic finding is normal, and only a microscopic examination reveals pathology. The dominant symptom is diarrhoea as well, often during the night. This condition is not typical of older age (rather in the middle age) but appears even in the elderly and we must be aware of it.

False diarrhoea

False diarrhoea develops in the case of faecal impaction and is connected with the development of faecaloma. Faecal impactions occur in both genders at any age but are particularly concentrated in the institutionalised or impaired elderly. The clinical consequences may be disabling and occasionally life-threatening. Stools stagnate usually in the rectum and older patients cannot excrete them. Clinical manifestations include faecal incontinence, abdominal distention and pain, anorexia, weight loss, intestinal obstruction, and stercoral ulceration with bleeding or colonic perforation. Chronic irritation causes watery and mucous secretion. This discharge (caused by mucosal irritation) often leaves spontaneously and can look like diarrhoea. Improper antidiarrhoeal treatment worsens this situation even more. The diagnosis begins with recognition of possible faecal impaction and confirmation by digital examination or abdominal radiography. Management consists in disimpaction, colon evacuation, and a maintenance bowel programme to prevent recurrent impactions [10].

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FOREKNOWLEDGE AS AN ASSOCIATED FACTOR FOR ADHERENCE TO THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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ABSTRACT

The goal of our essay is to evaluate the privity of patients suffering from inflammatory bowel disease (IBD) with regard to the essence of their disease, risk factors, and present ways of treatment including its side effects. Eighty patients with IBD (58 with Crohn's disease and 22 with ulcerative colitis, 40 males and 40 females) were included in our research and asked to fill in our anonymous questionnaire. It consisted of several parts: diet, possibilities of medicamentous therapy with its side effects, and timing of surgical therapy. In the end they assessed the level of their knowledge and named the resources from which they drew their information. It was concluded that 96 % of patients consider themselves sufficiently and correctly cognisant of their disease, but according to our evaluation the real number is lower than 52 %. In particular, the knowledge of the side effects of ongoing treatment was found to be inadequate. We assume that limited knowledge or misinformation might participate in the origin and development of non-adherence to therapy.

ABBREVIATIONS USED

IBD – inflammatory bowel disease
CD – Crohn's disease
UC – ulcerative colitis
5–ASA – 5–aminosalicylates

INTRODUCTION

Inflammatory bowel disease (IBD) refers to two related yet different diseases – Crohn's disease and ulcerative colitis. Both diseases cause chronic inflammation of the intestinal tract, which leads to a variety of symptoms. Crohn's disease may affect any part of the gastrointestinal tract and the inflammation penetrates all layers of the bowel wall. Ulcerative colitis affects the large intestine and the inflammation forms in the

lining of the colon. It may also cause damage to extraintestinal organs – joints, eyes, skin, liver, and lungs. IBD is a lifelong disease with periods of active inflammation in a part of the intestine (relapse) alternating with periods of disease control with mucosal healing of the intestine (remission).

The aetiology of IBD remains unknown and is most likely multifactorial. According to a wide range of studies, external agents significantly contribute to IBD manifestation (especially the presence of an infection, eating habits, smoking, hormonal contraception, and psychological pressure). Both diseases reach their spikes in two periods: the first is at the time of puberty and early adulthood and the other between 50–70 years of age. In the Czech Republic there are 3 to 5 out of 100,000 people suffering from Crohn's disease and 3 out of 100,000 suffering from symptomatic ulcerative colitis [1].

The therapy of IBD is only symptomatic and may be divided into conservative approach and surgical intervention. The conservative therapy includes medicaments, endoscopic therapy, nutritive and psychological intervention. The main goal of medicamentous therapy is to suppress the inflammation, provoke mucosal healing, and prolong the remission. There are several basic medicament groups used in medicamentous therapy – a suitable group is chosen according to the extent of the damage to the intestinal system and disease activity.

5–Aminosalicylates (5–ASA), immunosuppressives (corticosteroids, azathioprine, methotrexate, cyclosporine) [2] and biological therapy are used.

According to the available studies only 40 % of all patients are completely adherent to therapy [3]. Most authors agree that adherence is a complex problem. We assume that one of the key factors influencing adherence in patients is the quality of their foreknowledge - in other words understanding the essence of their disease and its cure.

METHODS

Eighty patients with inflammatory bowel disease participated in the study (40 males and 40 females, 58 patients with Crohn's disease and 22 patients with ulcerative colitis). The average age of the patients was 32 years and the average time of disease duration was 7 years. Thirty-one patients achieved primary education, 44 secondary education, and 5 were university educated.

They were asked to fill in an anonymous questionnaire, which was divided into several parts. The first was focused on basic demographic data (age, gender, achieved education, time duration of disease, and current therapy). The second part was devoted to diet. We aimed to find out how important it was for our patients and what kind of food they considered to be inappropriate. The third part was focused on various kinds of therapy. In case of medicamentous therapy we were primarily interested in the patients' knowledge of the side effects of their therapy. They were supposed to describe the side effects they were afraid of. In case of surgical approach we aimed to find out how our patients felt about its timing and asset. We were also interested whether patients sought out complementary medicine and if they considered it beneficial. Finally the patients were asked if they used their medication regularly. In the end the patients assessed the level of their knowledge and named the resources from which they drew their information.

RESULTS

1. Diet and its significance for patients with IBD

According to our results, 92.5 % of women and 75 % of men think of eating healthy food as being very important and 91 % of women and 91 % of men really eat it.

Alcohol was chosen as the most inappropriate food by both women (95 %) and men (100 %), wholemeal pastry by 73 % of women and black coffee by 62 %. Men chose black coffee in the second place with 62 % and grease in the third with 41 %.

2. Conservative IBD therapy

Ninety-three per cent of women and 78 % of men with CD and 66 % of women and 92 % of men with UC qualify their disease as incurable.

Altogether 82.5 % of women and 70 % of men with IBD are afraid of the side effects of their medication.

Eighty patients were cured with 5–aminosalicylates and corticosteroids. Thirty-nine per cent of women using 5–ASA are not afraid of any side effects, 35.5 % are afraid of teratogenic influence, 32 % of hepatotoxicity, and 29 % of nephrotoxicity. Sixty-three per cent of men are afraid of hepatotoxicity, 33 % of nephrotoxicity. Sixty-four per cent of women and 71 % of men using steroids are afraid of osteoporosis, 46 % of women and 54 % of men of hepatotoxicity.

Fifty-nine patients were treated with azathioprine. Altogether 54.5 % of women and 39 % of men are afraid of haematotoxicity, 45.5 % of women and 52 % of men of hepatotoxicity.

Twenty-nine patients were treated with cyclosporine. Forty-four per cent of women are afraid of teratogenic influence, hepatotoxicity and haematotoxicity, 22 % of nephrotoxicity. Forty per cent of men using the same cure are afraid of haematotoxicity and nephrotoxicity.

Twenty-six patients were treated with methotrexate. Eighty-six per cent of women from this sample are afraid of hepatotoxicity and 71 % of teratogenic influence. Forty per cent of men are afraid of hepatotoxicity; none of them is afraid of any side effects.

3. Possibilities of surgical intervention
It was concluded that 90 % of women and 87.5 % of men consider surgical intervention to be the last resort.

4. Complementary medicine
Sixty per cent of female patients and 37.5 % of male ones consider complementary therapy (homeopathy, acupuncture) as beneficial.

5. Regularity of using prescribed medication
Altogether 82.5 % of female patients and 67.5 % of male patients use their medication regularly according to the doctors' recommendation. A total of 12.5 % of male patients terminate their treatment when their condition improves.

6. Resources from which our patients drew their information
Ninety per cent of men indicated their doctor, 37.5 % named booklets they acquired at the doctor's, and 30 % mentioned the Internet. Altogether 72.5 % of women indicated their doctor as their resource, 67.5 % gained their information from brochures, 50 % from their co-patients, and 30 % from the Internet.

DISCUSSION

Several works were published in foreign literature pursuing the topic of non-adherence to medicamentous therapy of IBD. Sewitch and his colleagues determined conscious non-adherence in 36.5 of the patients [4], Lopez San Rom reached 35 % [5]. The ways of learning the measure of adherence to therapy are very complicated. D'Inca and his colleagues used the method of anonymous questionnaires and found conscious adherence in 39 % of the patients [6]. Červený et al. analysed samples of urine from patients treated with 5–ASA; there was no evidence of 5–ASA in 12.5 % of the patients [7].
We used the method of anonymous questionnaires in our research with patients of our gastroenterological clinic. However, most of them wished to fill in the form in our presence as they wanted to have the opportunity to discuss the questions. Therefore, we consider the evaluated questions to be very accurate and reflecting the real measure of foreknowledge of our patients.
The causes of medication non-adherence are multifactorial. We suppose that the quality of our patients' foreknowledge of their disease is closely linked with their adherence to the therapy.

CONCLUSIONS

Foreknowledge of patients with IBD concerning the essence of their disease and the possibilities of treatment is inadequate in the present times. While patients considered themselves to be well informed in 95 %, 50 % of their answers were incorrect. The major group of incorrect information was related to the side effects of ongoing treatment. As they have the deepest influence on non-adherence to therapy, we suggest that the Gastroenterological Society should actively participate in educational programmes and in elaboration of information for patients with IBD.

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SCREENING OF COELIAC DISEASE IN OSTEOPOROTIC PATIENTS

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INTRODUCTION

Coeliac sprue is traditionally understood as a disease related to early age. A certain part of the young population suffers from typical bowel symptoms, which belong to the group of active coeliac syndromes. Looking at the full-scale screening performed in European countries and in the US, we can see that the prevalence of this condition is about 1:100. This means that there are 40 000 to 50 000 people affected by coeliac sprue in the Czech Republic. However, only 15–20 % of the patients have been diagnosed and the rest of them remains undiagnosed. The main reason for this is subtle or even missing symptoms in the essential part of the patients (atypical or silent coeliac disease – see Table 1). Osteoporosis is the most frequent atypical manifestation of the disease in adulthood and in the elderly. The treatment is difficult particularly in women with a combination of coeliac disease and postmenopausal osteoporosis.

DEFINITION

Coeliac sprue (CS, coeliac disease, gluten-sensitive enteropathy) is a lifelong disease of the digestive tract. There is a strong association with the human leukocyte antigen (HLA) haplotype (DQ2 and DQ8), and consumption of gluten-containing cereals is necessary. Gliadin (the alcohol-soluble fraction of gluten), by means of presentation to the helper T cells, initiates an immunologically mediated and inappropriate inflammatory response, which leads to damage of the intestinal mucosa (mostly duodenal and jejunal) resulting in malabsorption. At the same time, a high amount of highly specific antibodies (AtATG – antibodies against tissue transglutaminase) is being generated.

EPIDEMIOLOGY

On average, the prevalence of coeliac disease in Western countries is supposed to be 1:100. The male-to-female ratio

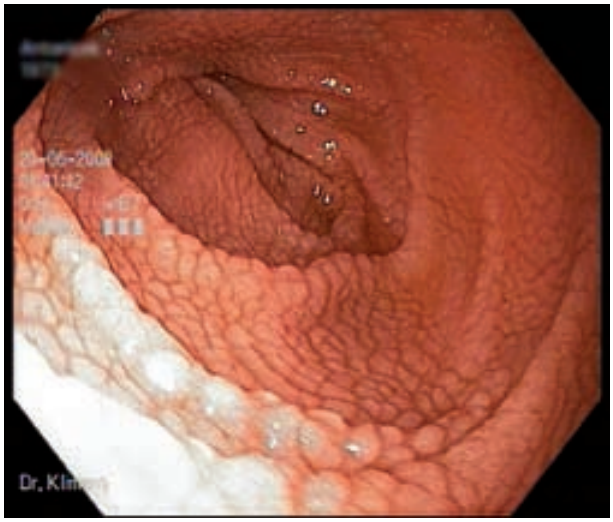

Figure 1
Atrophic duodenal mucosa

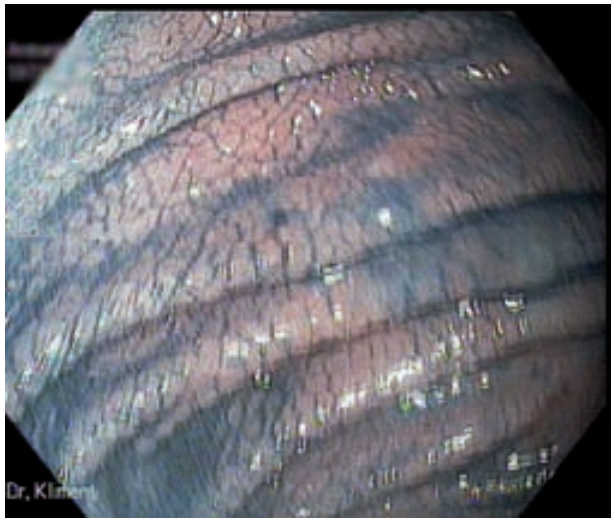

Figure 2
Appearance of atrophic duodenal mucosa after indigocarmine staining

is about 1:2. Coeliac disease has a strong hereditary component. The prevalence of the condition in first-degree relatives is approximately 8–18 %. Concordance in monozygotic twins approaches 70 %. The estimated frequency of coeliac disease in the Czech Republic is 1:200–250. Thus, there live here approximately 40 000 to 50 000 affected people.

CLINICAL PRESENTATION

The clinical picture of coeliac disease tends to be different depending on the age of the patient. The course of the disease is also influenced by genetic dispositions, duration of gluten exposure, and the degree of mucosal affection. Coeliac disease is no longer a rare condition affecting mostly children and causing only diarrhoea, weight loss, and anaemia. Its manifestation changes with age, gastrointestinal symptoms weaken, and extraintestinal manifestations play a more important role. The disease is mostly detected between the 30th and 40th year of age, later diagnosis is quite rare. After the 60th year of age, coeliac disease is not considered at all, as there are usually more frequent and urgent conditions to treat. The commonest symptoms that we observe in adulthood are minimal gastrointestinal troubles (flatulence, lack of appetite), fatigue and/or atypical extraintestinal symptoms – primarily osteoporosis with a severity not corresponding to age, anaemia, neurological and psychological disruptions. Glossitis, aphthous stomatitis, skin disorders, alopecia, amenorrhea, infertility, and impotence are less common troubles.
Osteopenia and osteoporosis are some of the most serious atypical manifestations of the disease in adulthood and in the elderly. Altogether 18–24 % of patients suffer from osteopenia, 34 % of postmenopausal female patients have osteoporosis in the lumbar area, and 27 % in the area of the femoral neck. Bone metabolism is mostly disturbed by malabsorption of nutrients with subsequently restricted calcium distribution, by a lower amount of vitamin D, growth hormone, and the insulin-like growth factor 1 (IGF-1).

DIAGNOSTICS

When considering coeliac disease in adulthood, we base our diagnosis on three factors:
1) Clinical picture as described above.
2) Serological markers – AtTGA (antibodies against tissue transglutaminase) with a sensitivity of 90–98 % and a specificity of 95–97 %, EMA (antiendomysial antibodies), AGA (antigliadin antibodies). Thanks to its high accuracy, good price and availability, AtTGA is the most suitable marker.
3) Biopsy of the small intestine mucosa. In common practice it means an endoscopically obtained sample of the mucosa of the aboral duodenum. The advanced stages of villous atrophy can be visible during endoscopy with the naked eye. Histologically, mucosal damage is evaluated according to the Marsh classification (stage 0–4), and stage 3 is the most typical for coeliac disease.

CLASSIFICATION

Because of the high frequency of non-characteristic symptoms coeliac disease is underdiagnosed in most of the

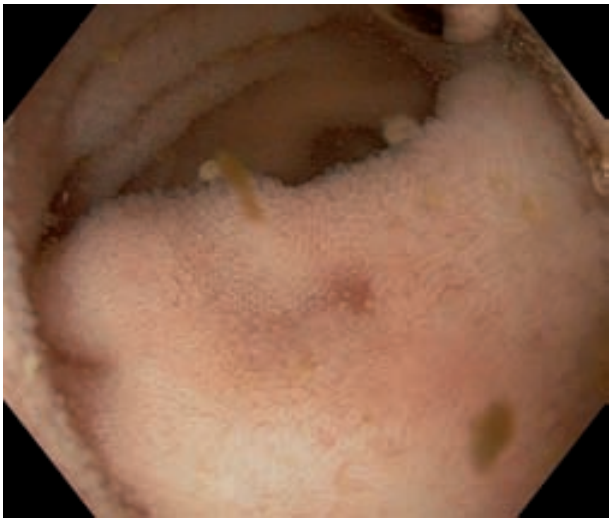

Figure 3
Normal appearance of duodenal mucosa

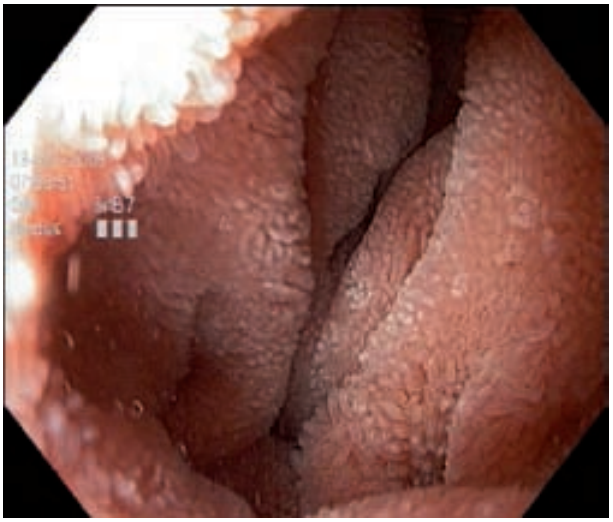

Figure 4
Normal appearance of duodenal mucosa in water immersion

affected people. This supports the concept of the "coeliac iceberg" – the smaller part above the surface represents the active forms of the disease. The essential part of the patients remains under water und thus undiagnosed.

Typical form. It represents about 30 % of the patients. Serological and histological markers are present, gastrointestinal symptoms dominate.

Subclinical (atypical, extraintestinal) form. Serological and histological markers are present. Atypical extraintestinal symptoms (anaemia, osteopathy, neurological and gynaecological symptomatology) prevail.

Silent form of CD. Serological and histological markers are present. Clinical symptoms are absent. Some of the patient's relatives can be affected by coeliac disease.

Latent form of CD. Specific antibodies are found. Histologically, there is only an increased number of IEA (intraepithelial lymphocytes) without atrophy. Clinical symptoms are missing. These patients are at risk of developing coeliac disease in the future. Genetic examination (HLA) is recommended.

COMPLICATIONS CAUSED BY CD

The most fatal complication of coeliac disease in adulthood and in the elderly is osteoporosis. In female patients osteoporosis associated with coeliac disease often combines with postmenopausal osteoporosis. In the Czech Republic, 15 % of men and 33 % of women older than 50 years and 39 % of men and 47 % of women older than 70 years suffer from osteoporosis. The clinical importance of osteoporosis consists mainly in its consequences, which are represented by fractures of both axial and appendicular skeleton. The most frequent are compressive fractures of vertebras, femoral neck, and radius. Such complications worsen the quality of life and often lead to its premature end. The mortality of women with a diagnosed fracture of the femoral neck is by 15 % higher than that of the other women. This mortality reaches up to 30 % in women older than 65 years.

Another extraintestinal manifestation in adulthood is anaemia caused by deficiency of iron, folate, pyridoxine, and

Table 1
Coeliac disease classification (FH = family history)

↑ IELγ/δ = ↑ intraepithelial γ/δ lymphocytes					
CS forms	**Typical**	**Silent**	**Latent**	**Potential**	**Subclinical**
Symptoms	+	– (FH)	-	often	atypical
Histology	+	+	↑ IELγ/δ	↑ IELγ/δ or -	+
Serology	+	+	+	+ or -	+

vitamin B12. Furthermore, there could be gynaecological (infertility, dysmenorrhoea, abortions), psychological (anxiety, depressions), and neurological symptoms (polyneuropathy, tetany, fatigue, brain atrophy, seizures). The most lethal of them is, fortunately scarce, intestinal lymphoma.

TREATMENT AND FOLLOW-UP

The treatment of coeliac disease is very simple. The patients have to adhere to a gluten-free diet for life. During the initial 3–6 months the intestinal mucosa is being restored. This process can be supported by substituting vitamins of B group and trace elements. Once the diagnosis is established it is recommended to substitute calcium in doses of 1000 mg per day and vitamin D in doses of 1600 IU per day (e.g. 4 drops of Vigantol per day or 20 drops once a week) in the first year of treatment and then to adapt to the results of densitometry. There are no data concerning the doses of the abovementioned medication. However, vitamin D seems to play a crucial role. In children the bone mineral density (BMD) is normalised within 3 years of the strict removal of gluten from the diet. On the contrary, in adulthood BMD usually does not reach its original value, especially in patients with secondary hyperparathyroidism in the initial stage. Densitometry is advisable immediately after establishing the diagnosis and then after a year of treatment. Diphosphonates are actually considered as the most suitable medication for the osteoporosis treatment. Strontium preparations seem to be promising as well.

SCREENING OF THE TARGET GROUP IN ADULTHOOD AND IN THE ELDERLY

In co-operation with an osteology centre in Zlín we examined a serological marker of coeliac disease (AtTGA) in 1409 patients. Thirteen patients were positive and gastroduodenoscopy with duodenal biopsy followed in all of them. The histology revealed atrophy of the duodenal mucosa of stage III a-b according to the Marsh classification. The total prevalence of coeliac disease in our group was then 1:100. We divided the group into two subgroups: A (younger than 55 years) with the prevalence 1:1.28 and B (older than 55 years) with the prevalence 1:100. None of them had typical bowel symptomatology. Five patients complained of intermittent diarrhoea and eight had occasional abdominal distension. We hereby confirmed the high prevalence of coeliac disease in the population of osteoporotic patients in the Czech Republic–1:100, which is twice as high as in the common population. However, in patients over 55 the prevalence is 1:28, which means 4 times higher than in the common population. Therefore, it is recommendable to screen all osteopenic and osteoporotic patients younger than 55 years for coeliac disease. Osteoporotic patients older than 55 years should be screened if they do not respond to the treatment adequately or show even minimal intestinal symptomatology. In this way we can improve the prognosis of patients suffering from coeliac disease and associated osteoporosis.

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ABSTRACTS OF SELECTED PAPERS PRESENTED AT THE XVIth CONFERENCE OF YOUNG PHYSICIANS, ST. ANNE'S FACULTY HOSPITAL IN BRNO, 24 JUNE 2009

Z. Trávníčková (Department of Clinical Immunology and Allergology, St Anne's Faculty Hospital, Faculty of Medicine, Masaryk University, Brno): **Investigation of antibody production after antigen challenge in patients with common variable immunodeficiency (CVID) by ELISPOT**

Common variable immunodeficiency (CVID) is one of the most common immunodeficiencies. It is characterised by low serum levels of IgG, IgA, normal or low levels of IgM, and impaired antibody response. Despite intensive research the real cause of these diseases and involvement of B cells remain unclear. The goal of the study was to determine the ability of antibody response after vaccination in CVID patients.

The use of ELISPOT (enzyme-linked immunosorbent spot) assay permits detection of antibody production on the cellular level. It may detect the antibody response in patients under immunoglobulin substitution. Thirty-seven CVID patients were vaccinated with tetanus toxoid (TAT) and pneumococcal polysaccharide (PCP) vaccine. Fifty healthy individuals were boosted with TAT, ten received pneumococcal polysaccharide vaccine alone, and twenty-one were immunised with both vaccines together. All volunteers were examined before vaccination, on day 7 after vaccination, and 4 to 11 weeks after vaccination by the ELISPOT assay.

The median of spot-forming cells (SFC) in healthy volunteers was found to be for tetanus toxoid 9 882 (IgG), 532 (IgA), 0 (IgM), and for pneumococcal polysaccharide 3 870 (IgG), 35 200 (IgA), 10 087 (IgM) SFC/10^6 B cells. In contrast to this, there was nearly no specific antibody production against protein or polysaccharide antigens in IgG, IgA, and IgM immunoglobulin classes in the CVID patients. If any specific IgG production was detected, most of them (3 patients) belonged to the group smB+21^{norm} (altogether 7 patients) according to the EUROclass classification, while in the remaining groups a response was observed only exceptionally.

The ELISPOT technique is a useful functional test for the detection of specific antibody response in patients under substitution immunoglobulin therapy. Our results may help to better elucidate the antibody production defects in CVID patients.

This work was supported by grant No. NR 9035–4 of the Czech Ministry of Health.

O. Tichá, M. Štouračová (Department of Clinical Immunology and Allergology, St Anne's Faculty Hospital, Faculty of Medicine, Masaryk University, Brno): **Expression of CD38 on the lymphocytes of kidney transplant patients**

Cytomegalovirus (CMV) infection is a life-threatening complication of patients after solid organ transplantation. It appears in the first months after transplantation as a consequence of the use of immunosuppression.

The study was performed in the Centre of Cardiovascular and Transplant Surgery (Brno, Czech Republic) in the period from December 2002 to April 2008, when 237 patients underwent renal transplantation. The patients were monitored at the time of their hospitalisation 2–3 months after transplantation. The percentage of CD38^{high} cells from Tc lymphocytes estimated by flow cytometry, the titre of anti-CMV IgM antibodies determined by the ELISA method, and the number of CMV copies in peripheral blood using real-time polymerase chain reaction (RT-PCR) were monitored in these patients.

Between 31st and 63rd days after transplantation 12 patients (5 %) were diagnosed with CMV infection. These patients had increased percentage of CD38^{high} from CD3+CD8+ T lymphocytes above the arbitrary limit of 20 %. Eight of them had an increased level of CD38^{high} above 20 % from 3 to 32 days before the CMV infection was diagnosed and antivirotics were administrated.

The follow-up of CD38^{high} percentage from CD3+CD8+ lymphocytes seems to be a useful additional diagnostic marker for patients after kidney transplantation.

S. Zgažarová[1], Z. Trávníčková[2] ([1]1st Department of Dermatovenereology, Faculty of Medicine, Masaryk University and St. Anne's Faculty Hospital, Brno, [2]Department of Clinical Immunology and Allergology, Faculty of Medicine, Masaryk University and St. Anne's Faculty Hospital, Brno): **Drug hypersensitivity to tribenoside (Glyvenol)**

Tribenoside is a semisynthetic sugar derivative. It is widely used as Glyvenol (capsules) and Procto-Glyvenol (cream or suppositories). It is indicated for the treatment of chronic venous insufficiency, haemorrhoids, and arthritis because of high affinity to the vessel wall and a wide spectrum of pharmacological effects including venotonic, antioedemic, fibrinolysis-promoting, analgesic, antiinflammatory, antiallergic, membrane stabilising, and bactericidal ones.

Up to 10 % of patients treated with tribenoside can suffer from skin side effects. They usually occur as anaphylaxis, angio-oedema, urticaria, and exanthemas (the most common

maculopapular rash). The pathogenesis of cutaneous adverse drug reactions (CADR) induced by tribenoside is unknown. No universal test for a final diagnosis of CADR with 100% sensitivity and specificity has existed as yet.

We evaluated 27 inpatients treated in our Dermatology department for exanthemas induced by tribenoside in the period from October 2005 to August 2008. The patients were investigated to confirm the aetiology of exanthemas. On the basis of history, clinical features and course of disease we supposed a delayed reaction to tribenoside.

Twenty-two out of 27 patients were examined using a patch test from in vivo diagnostic methods. In vitro (laboratory) tests were performed in 8 out of 22 patients including the lymphocyte transformation test and the basophil activation test.

A positive patch test reaction to tribenoside was seen in 1 out of 22 patients. The basophil activation test gave a positive reaction in 1 out of 8 patients. The lymphocyte transformation test elicited one border-positive reaction.

In spite of our study the results in patients with exanthemas exposed to tribenoside prove that immediate as well as delayed hypersensitivity reactions could occur. This finding is in accordance with the clinical picture of exanthemas, which are not uniform, either.

H. Škvařilová (Department of Dentistry, St. Anne's Faculty Hospital, Faculty of Medicine, Masaryk University, Brno): **The sealing quality of filling materials used in dentistry**

The aim of this study was evaluation of the sealing qualities of temporary filling materials in the crown part of extracted teeth.

The function of a temporary filling material in dentistry is twofold: first, to prevent the saliva with its microorganisms from gaining entrance into the root canal, thus preventing infection; second, to prevent medicaments placed into the pulp chamber from escaping into the oral cavity, thereby preserving the effectiveness of the intracanal medication.

Forty extracted teeth, which were fixed in 10% neutral formaldehyde, were examined. Before the experiment the teeth were washed in flowing water for 24 hours. Black's class I and V cavities were prepared. The teeth were filled up with one of the following materials:

- Zinc-oxide sulphate cement (Providentin)
- Material based on plaster and organic cement (Provimat)
- Caviton
- Cavit W
- Zinc-oxide eugenol cement (IRM cement)
- Glass-ionomer cement (GC Fuji)
- Glass-ionomer cement (Ketac Fill plus)
- Zinc-oxide eugenol cement (Caryosan)

The entire tooth surface, except for a cavity area, was coated with a thick layer of nail polish. After immersing in a solution of methylene blue for 24 hours, the teeth were longitudinally sectioned and fractured, and examined under a stereo magnifying lens under magnification of 10.

The results show that the most effective penetration of materials used was noticed with zinc-oxide eugenol (Caryosan) and zinc-oxide sulphate (Providentin) both in the fissure and in the filling material proper.

The best results were reached with glass-ionomer cement (GC Fuji) and Caviton.

The existing numbers of samples studied do not allow statistical evaluation but show noticeable differences between the materials used.

The results of this study serve as a recommendation for the right choice of filling material.

J. Nechvátalová, M. Vlková (Department of Clinical Immunology and Allergology, Faculty of Medicine, Masaryk University, St. Anne's Faculty Hospital, Brno): **Time-related stability of abnormalities in B lymphocyte subpopulations in patients with common variable immunodeficiency (CVID)**

Common variable immunodeficiency (CVID) is a heterogeneous immunodeficiency disease characterised by a low level of serum immunoglobulins with various degrees of clinical immunodeficiency manifestation. Previous studies have shown various abnormalities in lymphocyte subpopulations; the patients had a reduced number of terminal stages of B-cell development. The presence of these B-lymphocyte abnormalities is the principle of the laboratory classification scheme called EUROclass.

The goal of this study was to disclose to what degree these abnormalities were constant. Phenotyping was performed by flow cytometric analysis in 25 patients (aged 46±15 years). We compared representation of certain B-lymphocyte subpopulations in two measurements in the course of 2 to 3 years. Statistical analysis was performed by means of the Wilcoxon signed rank test.

The results showed an increase in the relative number of $CD27^{+}$ cells ("mature" B lymphocytes) (P=0.008) as well as $CD21^{low}38^{low}$ (P=0.012), whereas the IgD+CD27 subpopulation ("immature" B lymphocytes) did not change (P=0.2473).

These results may show that lymphocyte subpopulation abnormalities seen in CVID patients are not constant and tend to "normalisation".

G. Jamborová[1], P. Nachtigal[2], K. Pospěchová[2], N. Pospíšilová[2], V. Řeháček[1], V. Semecký[2] ([1]Transfusion Department, University Hospital Hradec Králové, [2]Biological and Medical Sciences

Department, Faculty of Pharmacy in Hradec, Charles University in Prague, Hradec Králové): **MDOC™ effects on acute dermal wound healing in an experimental rat model**

The occurrence of hard-to-heal wounds is very frequent, especially when associated with other diseases. Moist wound healing is an effective way of even complicated cases of treatment and is represented by various dressing products with appropriate properties. Microdispersed oxidised cellulose (MDOC™), a patent of Alltracel laboratories (Dublin, Ireland), is a random copolymer of polyanhydroglucose and polyanhydroglucuronic acid. MDOC™ was identified to be effectively used as a biocompatible and completely absorbable haemostatic agent. This material exhibits low toxicity and is usually administered in powder, spray, gel or textile form. Furthermore, MDOC™ can be employed as a polymeric ion or drug carrier (ATBs).

The aim of our study was to investigate the effect of locally applied distinct forms of MDOC™ on acute cutaneous wound healing in an experimental rat model. Male Wistar rats were divided into four tested MDOC™ groups and one control group. A central defect (1 cm in diameter) was made in the paravertebral area and the appropriate amount of MDOC™ tested form (powder, gel, textile, and spray) was implanted in the wound base. For the observation of wound contraction several techniques were exploited; in particular gross pathology, light microscopy, and immunohistochemistry technique for the detection of specific marker (TNFRI, CCR2, TGF-β RII) expression changes in all phases of wound healing.

Our results (obtained on days 3, 7, and 14 after injury) showed that the application of any MDOC™ form did not lead to any significant differences. The substance under study displayed haemostatic action and localisation of cell infiltrate detectable in the new tissue in the dermis. Additionally, immunohistochemical analysis did not prove any significant influence of MDOC™, either. The presence of TNFRI, CCR2, and TGF-β RII was detected in the dermis being expressed by inflammatory cells, by endothelial and epidermal cells in the MDOC™ groups as well as in the control group. Other investigations focusing on specific inflammatory markers (e.g. CD 68, FSP 1) in the wound must be accomplished to clarify precise effects of MDOC™ forms.

I. Kajzrlíková[1], P. Vítek[1], J. Chalupa[1], A. Hájek[2], J. Platoš[1], J. Kuchař[1], P. Řeha[1] ([1]Beskydy Gastrocentre, Department of Internal Medicine, [2]Beskydy Gastrocentre, Department of Surgery, Frýdek-Místek Hospital): **THE FAMILY PROJECT – the first experience with direct colonoscopic screening for first-degree relatives of colorectal cancer and advanced adenoma patients**

The first-degree relatives of patients with colorectal cancer or advanced adenoma have a higher risk of colorectal neoplasia. The primary colonoscopic screening and subsequent follow-up are unambiguously recommended for them. The authors decided to systematically reach out the first-degree relatives in THE FAMILY PROJECT and thus provide adequate screening for this high-risk group. The project was initiated in July 2008 and it has still been running. The patients with colorectal cancer or advanced adenoma are informed in a personal interview and asked for their first-degree relatives' phone numbers. The relatives are contacted and invited to the Project clinic. In accordance with the age and the individual risk of the relatives the colonoscopy is planned. There have been 87 patients with colorectal cancer or advanced adenoma included in the Project until the end of April 2009. Subsequently, 183 first-degree relatives were contacted and out of them 76 (42 %) have already visited the Project clinic. Sixty-five first-degree relatives were eligible for colonoscopic screening at the time of attendance, 13 of them have already undergone colonoscopy, 10 of them have already had screening, but the method was not appropriate (FOBT), 42 (65 %) of them have not participated in any kind of screening yet. Until the end of April 2009, 43 relatives had undergone colonoscopy within the Project, 17 neoplastic lesions were found and removed, out of them 7 advanced adenomas. The majority of first-degree relatives are either unscreened or screened with an inappropriate method (FOBT). Direct personal counselling of first-degree relatives seems to be effective and can significantly improve compliance of these patients with colonoscopic screening. We have found and removed advanced neoplastic lesions in this group of patients.

Complied and revised by J. Litzman

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XXVIth Conference of the Czech Society of Hypertension (ČSH), XVIIIth Conference of the Preventive Cardiology Working Group of the Czech Society of Cardiology (ČKS) and XIVth Conference of the Heart Failure Working Group of the ČKS

Mikulov, October 1 to 3, 2009

A meeting of Czech physicians specialising in the issues of high blood pressure traditionally took place at the beginning of October in the attractive environment of Mikulov Castle. Information useful for clinical practice was exchanged not only among physicians but also, for the fourth year running, among nurses working in this field.

Interest in the diagnosis and treatment of hypertension, one of the most frequent cardiovascular diseases, was also confirmed by the participation of a number of foreign experts. It is becoming clear that attaining target blood pressure values in patients remains a topical medical problem even in the 21st century.

The introductory block of lectures was opened by Prof. Miroslav Souček, MD, Ph.D., the chairman of the conference organising committee and Prof. Jiří Widimský Jr., MD, Ph.D., the chairman of the Czech Society of Hypertension (ČHS). The results of the joint **KOHYBA study** were presented at this venue for the first time. Prof. Václav Monhart MD traditionally dedicated his contribution to the level of control of **hypertension in patients with chronic renal disease.** The group of authors from IKEM (Institute of Clinical and Experimental Medicine), Prague (Bürgelová et al) presented the results of the 5-year follow-up of **living kidney donors**, whose aim was to determine the incidence of hypertension and eventual end-organ complications in these subjects. According to the authors, kidney donation is safe, despite the incidence of hypertension (this was 30% at the beginning of follow-up and 52% at the end of follow-up). Jiří Ceral MD drew attention in his lecture **Malignant Hypertension in the 21st Century** to the fact that even in this age, though it remains a rarity, one may face this most serious form of severe hypertension with end-organ damage in clinical practice. Changes on the eye-ground are considered to be diagnostic in such cases. According to the author, today this entity represents one due to "neglected" hypertension, with patients nearly always being guilty of such neglect. Therapeutic success may be achieved today even in this distinctive form of hypertension with the help of available drugs.

Mikulov castle - conference venue

Prof. Jiří Widimský jr., MD, Ph.D.

Prof. Miroslav Souček, MD, Ph.D.

In the Hot Lines Block dedicated to the BEAUTIFUL study, Prof. Jiří Vítovec, MD Ph.D. presented in his lecture the results of the sub-analysis of symptomatic patients. This study involved the first evaluation of the effects of the sole decrease of cardiac frequency using ivabradine on the incidence of cardiovascular events in patients with CAD and left ventricular dysfunction.

In the next part of this block of lectures, Prof. Jindřich Špinar, MD Ph.D. presented in detail the ONTARIO I and II studies. Both surveys monitored the long-term clinical state of patients receiving various types of ACE inhibitors (ACEi). The first retrospective survey followed the fate of patients who received ACEi during hospitalisation for myocardial infarction (MI) or later- within one month of the MI- as part of secondary pharmacological prevention. The second survey similarly followed the fate of a large number of patients with chronic heart failure treated with various ACEi.

In Mikulov, the ČSH also introduced the Czech version of the HeartScore® program – the electronic and interactive version of the SCORE risk tables created and developed for the Czech Republic on the basis of mortality data from ÚZIS (Institute of Health Information and Statistics of the Czech Republic) and data regarding the basic risk factors of cardiovascular disease