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SCIENTIFIC PROGRAM

Thursday, December 8, 2005

08:00 Registration, Coffee / Tea and Visit the Exhibition

08:30 - 09:00 Opening Session

WELCOMING REMARKS

M.M. Krausz, Chairman, Israel Surgical Association
Y. Ziv, Chairman, Israel Society of Colon and Rectal Surgery, Conference Chairman

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09:00 - 10:30 Session I **INVITED LECTURES**

Chairpersons: **M.M. Krausz**, Israel
R. Weil, Israel

09:00 GUIDELINES AND QUALITY CONTROL IN COLORECTAL SURGERY
B. Shpitz, Sapir Medical Center, Meir General Hospital, Kfar Sava, Israel

09:25 FAMILIAL ADENOMATOUS POLYPOSIS
R.K.S. Phillips, St. Mark's Hospital and Imperial College, School of Medicine, London, UK

09:50 THE ROLE OF HISTOPATHOLOGY IN THE MANAGEMENT OF MALIGNANT COLORECTAL POLYPS
H.S. Cooper, Dept. of Pathology, Fox Chase Cancer Center, Philadelphia, PA, USA

10:15 Discussion

10:30 *Coffee Break and Visit the Exhibition*

11:00 - 12:00 Session II **FREE PAPERS**

Chairpersons: **D. Neufeld**, Israel
A. Rosen, Israel

11:00 DOES THE EXTENT OF PATHOLOGIC RESPONSE TO NEOADJUVANT CHEMORADIATION FOR ADVANCED RECTAL CANCER INFLUENCE LOCAL RECURRENCE AND SURVIVAL?
H. Tulchinsky, E. Shmueli, A. Figer, R. Geva, G. Goldman, M. Inbar, J.M. Klausner, M. Rabau
Dept. of Surgery B and Oncology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

11:10 IS TRANSANAL ENDOSCOPIC MICROSURGERY A VALID TREATMENT FOR T2 RECTAL TUMORS?
N. Issa[1], M.M. Krausz[2], S.D. Duek[1]
Colorectal Unit[1], Dept. of General Surgery A[2], Rambam Medical Center and Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel

11:20 ONE-STAGE LAPAROSCOPIC COLORECTAL RESECTION AFTER PLACEMENT OF SELF-EXPANDING METALLIC STENTS FOR COLORECTAL OBSTRUCTION – A PROSPECTIVE STUDY
A. Mahajna[1,3], P. Wintringer [1], R. Beyssac[2], C. Barbaris[2], T. Patrice[2], J.-L. Dulucq[1]
Dept. of Abdominal Surgery[1] and Dept. of Gastroenterology[2], Maison de Santé Protestante, Bagatelle Hospital, Talence-Bordeaux, France, Dept. of General Surgery A[3], Rambam Medical Center, Haifa, Israel

11:30 REAL TIME-POLYMERASE CHAIN REACTION (PCR) IMPROVES SENSITIVITY OF LYMPHATIC STAGING IN COLON CANCER PATIENTS
R. Grinbaum[1], A.O. Gure[4], M. Roycetacher[1], I. Eisenberg[2], G. Ritter[4], L.J. Old[4], H.R. Freund[1], T. Peretz[3], S. Mitrani-Rosenbaum[2], **A. Nissan**[1]
Dept. of Surgery[1], Molecular Biology[2], Oncology[3], Hadassah Hebrew University Medical Center, Mount Scopus, Jerusalem, Israel, Ludwig Institute for Cancer Research[4], New York, NY, USA.

11:40 CROSSLINKED CHITOSAN IMPLANTS AS POTENTIAL DEGRADABLE DEVICES FOR BRACHYTHERAPY: *IN VITRO* AND *IN VIVO* ANALYSIS
B. Orkin[1], A.K. Azab[2], A. Nissan[3], M. Klein[1], M. Srebnik[2], A. Rubinstein[2]
[1] Hadassah University Medical Center, Ein Kerem, [2] The Hebrew University of Jerusalem, School of Pharmacy, [3] Dept. of Surgery, Hadassah University Medical Center, Mount Scopus, Jerusalem, Israel

11:50 Wrap-up

12:00 - 13:00 Session III **FREE PAPERS**

Chairpersons: **D. Duek**, Israel
H. Tulchinsky, Israel

12:00 ACCURACY OF ENDORECTAL ULTRASOUND IN THE PREOPERATIVE STAGING OF RECTAL ADENOMAS, T1- AND T2-CARCINOMAS
B. Person, D. Maron, R. Arya, J. Efron, D.R. Sands, A. Vernava III, E.G. Weiss, S. Wexner, J.J. Nogueras
Cleveland Clinic Florida, Weston, FL, USA

12:10 BEVACIZUMAB (AVASTIN) BASED NEOADJUVANT THERAPY FOR LIVER METASTASES OF COLORECTAL ORIGIN: AN ISRAELI MULTICENTER COLLABORATIVE STUDY OF THE ISRAELI GASTROINTESTINAL ONCOLOGY GROUP (IGOG)
D. Aderka[1,5], E. Shmueli[2,5], A. Figer[2,5], A. Beny[3,6], B. Klein[4,5] R. Catane[1,5]
for the IGOG with the collaboration of the hepato - biliary Surgery teams of Chaim Sheba Medical Center (A. Valeanu[1,5], M. Sarely [1,5]) the Tel Aviv Sourasky Medical Center (M. Ben-Haim[2,5], R. Nakache [2,5]) and Rambam Medical Center (R. Hadad), Divisions of Oncology of Chaim Sheba Medical Center[1], Tel Aviv Sourasky Medical Center [2], Rambam Medical Center[3], Meir Medical Center[4], Sackler School of Medicine, Tel Aviv University[5] and the Technion - Israel Institute of Technology, Haifa[6], Israel

12:20 LAPAROSCOPIC COLECTOMY FOR COLONIC POLYPS
A. Reshef, O. Zmora, D. Neufeld, D. Rosin, B. Benjamin, E. Klein, A. Ayalon, B. Shpitz
Depts. of Surgery, Chaim Sheba Medical Center, Tel Hashomer and Meir Medical Center, Kfar-Sava, Israel

12:30 SURGICAL TREATMENT OF COLORECTAL CANCER (CRC) PATIENTS WITH CLINICAL DIAGNOSIS OF HEREDITARY NON POLYPOSIS COLORECTAL CANCER (HNPCC)
Z. Levi[1], R. Hazazi[1], P. Rozen[1,2], Y. Niv[1,2]
Gastroenterology[1] Dept., Rabin Medical Center, Petach Tikva; Clalit Health Services (CHS), Tel Aviv & [2]Tel Aviv University Medical School, Israel

12:40 LIGASURE [TM] HEMORRHOIDECTOMY - LONG -TERM FOLLOW-UP USING A NEW SCORING METHOD
J. Sayfan, Y. Khromov, A. Becker, L. Koltun
Dept. of Surgery A, Haemek Medical Center, Afula, B. Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel

12:50 Wrap-up

13:00 *LUNCH BREAK*

14:00 - 15:30 Session IV **INVITED LECTURES**

Chairpersons: **S. Walfisch**, Israel
O. Zmora, Israel

14:00 RADIOTHERAPY AND CHEMO-RADIOTHERAPY FOR RECTAL CANCER. STATE OF THE ART 2005
R. Pfeffer, Radiation Oncology Unit, Chaim Sheba Medical Center, Tel Hashomer, Israel

14:25 MODERN SURGERY OF RECTAL CANCER
R.K.S. Phillips, St. Mark's Hospital and Imperial College, School of Medicine, London, UK

14:50 THE DEXTRAN SULFATE SODIUM MODEL OF MOUSE COLITIS - AN EXCELLENT MODEL FOR THE STUDY OF COLITIS ASSOCIATED NEOPLASIA AND ITS CHEMOPREVENTION
H.S. Cooper, Dept. of Pathology, Fox Chase Cancer Center, Philadelphia, PA, USA

15:15 Discussion

15:30 *Coffee Break and Visit the Exhibition*

16:00 - 16:40 Session V **PANEL DISCUSSION**

Chairperson: **M. Rabau**, Israel

Panel Members:
H.S. Cooper, USA
Z. Dreznik, Israel
R. Pfeffer, Israel
R.K.S. Phillips, UK
J. Sayfan, Israel
Y. Ziv, Israel

16:40 - 17:00 Session VI **INVITED LECTURE**

16:40 THE MEDICO-LEGAL IMPLICATIONS OF CLINICAL GUIDELINES IN COLO-PROCTOLOGY
O. Kaplan, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

17:00 CONCLUDING REMARKS
S. Walfisch, Israel

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FAMILIAL ADENOMATOUS POLYPOSIS

Robin Phillips, Consultant Surgeon and Dean, St Mark's Hospital, London, UK

Objectives

- interpret molecular biology testing in FAP and integrate into management
- determine which operation is most suitable for individual FAP patients depending on their genotype/phenotype
- distinguish between different severities of duodenal disease and review management

Introduction

Familial adenomatous polyposis (FAP) is an autosomal dominant condition caused by mutation of the APC gene which lies on the long arm of chromosome 5. Mutation may occur on any one of the 15 exons. The gene codes for a protein which seems to be important in cell-cell adhesion. Patients may be identified through their phenotype or through their genotype.

The FAP phenotype is characterised by more than 100 adenomatous polyps in the large bowel and often by many thousands. Characteristically there are also microadenomas, often known in the USA as aberrant crypt foci, which may be missed endoscopically unless dye-spray is used at colonoscopy. Most patients also have duodenal adenomas and about half of them have fundic gland polyps.

Congenital hypertrophy of the retinal pigment epithelium (CHRPE), sebaceous cysts and osteomas are frequently also seen, depending on the mutation position in the APC gene. Desmoid disease may arise in 10-15% of patients and are covered elsewhere by Mr Windsor.

Patients present either through screening of at risk individuals or symptomatically as new mutations. This gives a bimodal age distribution: teenage screen detected; early 30s presenting symptomatically (and frequently with cancer already present).

Diagnosis

In families where the mutation is known, mutation testing should be offered. Those testing positive should undergo dye-spray colonoscopy to determine their phenotype (dense or sparse polyposis, rectal sparing or rectal involvement), as this will aid surgical decision making. Those who are mutation negative may be discharged from follow-up. They should, however, be advised that they have the normal population risk of developing sporadic colorectal cancer, so they should not ignore colorectal symptoms just because they have a negative gene test.

Where gene testing is not possible, screening of at risk individuals commences around the age of 12 years. It is important for the clinician to be aware that acclimatising the patient to regular check-ups is probably more important than the assiduosness with which any one particular examination is performed. That is to say, over zealous attempts in an embarrassed 12 year old to obtain perfect views of the rectum may be met by subsequent lifelong refusal to attend. It is better to accept a sub-optimal clinical examination, especially in the young, and know that patient will still attend next year.

Most FAP patients will express the phenotype in the rectum. Those with attenuated disease may not, but then their cancer risk is reduced.

At St Mark's Hospital at risk individuals are screened annually be rigid or flexible sigmoidoscopy until the age of 20 years when the first dye-spray colonoscopy is performed. A negative dye-spray examination in a patient over the age of 20 years has not yet in our experience been followed by the later appearance of the phenotype. Despite this, and partly for audit and research purposes, we continue five-yearly dye-spray colonoscopy thereafter.

The surgical choices

None of the surgical options are without a downside. All are compromises: some, where the perceived risk of rectal cancer is low, compromise in terms of residual rectal cancer risk; others compromise in terms of function, complications and quality of life.

Proctocolectomy and ileostomy

This option should be reserved for patients presenting with an ultra-low rectal cancer in the presence of FAP. Otherwise it is included for largely historical reasons.

Colectomy and ileorectal anastomosis (IRA)

This was at one time the only operation which preserved anal continence.
It was therefore used in circumstances where today's surgeons would never dream of using it: for example, those with a high density phenotype or genotype - and in particular, those with a germline mutation at codon 1309.

When used appropriately, it has the advantage of low morbidity and good function. It particularly avoids the risks of pelvic dissection, which in a male may give rise to problems with erection or ejaculation, and which in females we are increasingly becoming aware that it leads to markedly reduced fertility.

It is probably best reserved for younger patients with low density disease and sparse or no rectal involvement.

Follow-up should be by six-monthly flexible endoscopic examination after two enemas. The risk of rectal cancer seems low under the age of 50 years but rises rapidly thereafter to 30%[1].

Proctocolectomy and ileoanal pouch formation

This is the operation of choice with a high density phenotype or genotype (and in particular, for the 1309 mutation). Complication rates are higher than for IRA and if anything function is marginally worse.

The particular recent concern has been the markedly reduced fertility rate in women who have had pouch surgery, not only for ulcerative colitis but also for FAP. Women wishing to have children should be counselled and may opt during their childbearing years for an IRA followed later by pouch conversion[2].

The hope that pouch surgery would remove the cancer risk from the evacuatory mechanism has been dashed in recent times by the high frequency of pouch polyposis as patients age (up to 70% in some series)[3] and a few reported cases of actual pouch cancer[4]. Thus pouches should continue under endoscopic surveillance.

The feasibility of an initial IRA followed later by pouch conversion should not be ruled out of court. Rarely it proves not possible because of unsuspected desmoid disease, and because of this is probably wise to perform an abdominal CT scan prior to surgery. In the majority where pouch conversion is possible, morbidity and function are equivalent to primary pouch surgery[5].

Special issues related to desmoid disease

There are some polyposis families where desmoid disease is particularly prevalent (see Mr Windsor's article elsewhere). These families tend to have a germline mutation 3' of codon 1444. Not infrequently the large bowel polyp burden and thus the colorectal cancer risk is low. In these families there may be a case for annual colonoscopy and treatment with celecoxib 400mg BD rather than prophylactic surgery[6].

The duodenum

Approximately 90% of FAP patients can be shown on side-viewing upper GI endoscopy to have duodenal adenomas. But only about 5% of them will die of duodenal cancer, so the cancer risk is much lower than for the large bowel. The phenotype/genotype correlations seen with large bowel polyposis do not seem to apply for duodenal disease. Thus patients with a mutation at codon 1309 are no more likely to have advanced duodenal disease than patients with other mutations. Endoscopists not acquainted with FAP may be quite startled by the often dense gastric fundic gland polyposis present in about 50% of patients. In general, these polyps can be ignored.

Spigelman staging and its relationship to prognosis

Duodenal polyposis is staged according to the number of duodenal polyps, their architecture (villous, tubulovillous, tubular) and the degree of dysplasia from Spigelman stage 0 - IV. A recent study has shown a 36% rate of duodenal cancer over 10 years in patients with stage IV disease and no more than a 2% risk with lesser stages[7].

Management of duodenal polyposis

Side-viewing upper GI endoscopy should be performed to visualise the ampulla commencing at age 25 years. Patients with stages 0, I, II disease should have screening 3-5 yearly. Those with stage III disease should currently be considered for advanced endoscopic management, probably allied with adjuvant treatment with celecoxib at a dose of 400mg BD[8], and be endoscoped six-monthly to one yearly. Those with stage IV disease should have an opportunity to discuss their management with an experienced upper GI surgeon with a view to some form of upper GI excisional surgery, such as pylorus preserving duodenectomy[9]. The balance here lies between the malignant risk over the next 10 years, offset by the upper GI surgeon's own track record in terms of surgical morbidity and mortality. Lesser forms of surgery, such as duodenotomy and polyp clearance, have an almost universal recurrence rate within one year and so have largely been abandoned[9].

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THE ROLE OF HISTOPATHOLOGY IN THE MANAGEMENT OF MALIGNANT COLORECTAL POLYPS

H.S. Cooper, Dept. of Pathology, Fox Chase Cancer Center, Philadelphia, PA, USA

The histopathological interpretation is extremely important in the management of the patient with an endoscopically removed malignant polyp. A malignant polyp of the colon or rectum is defined as a lesion in which cancer has invaded through the muscularis mucosae and into the submucosa (pT1). This process involves the technical handling of the specimen, communication with the endoscopist, and finally histopathological interpretation. The specimen requires an adequate time of fixation so that it can be sectioned properly. Communication with the clinician as to whether the specimen was removed in one piece or piecemeal is essential. The histopathological parameters that one traditionally examines are 1) status of the margin of resection, 2) grade of the cancer, and 3) lymphatic and/or venous invasion. Presently there is no consensus as to what defines tumor at or near a margin. Some investigators define this as tumor less than or equal to 1 mm, less than or equal to 2 mm, or cancer within the cautery of the transected margin. The incidence of adverse outcome (tumor metastatic to lymph nodes and/or residual tumor in the resection site) is approximately 20% in those malignant polyps with any unfavorable histological features (tumor at or near the margin or grade 3 cancer or lymphatic invasion) and 0% in those without unfavorable histopathological features. The interobserver variation is substantial to excellent for accessing grade and the status of the margin, but fair to substantial for diagnosing lymphatic invasion. Recently other investigators have reported; 1) depth of submucosal invasion ($\geq$ 2.0 mm), 2) the presence of tumor budding, and 3) depth of lymphatic invasion ($\geq$ 2.0 mm) as unfavorable histological parameters which are significantly associated with an adverse outcome. Patients with unfavorable histopathological features are probably best managed by resection post polypectomy, whereas in the absence of unfavorable histological features, polypectomy alone is adequate treatment.

DOES THE EXTENT OF PATHOLOGIC RESPONSE TO NEOADJUVANT CHEMORADIATION FOR ADVANCED RECTAL CANCER INFLUENCE LOCAL RECURRENCE AND SURVIVAL?

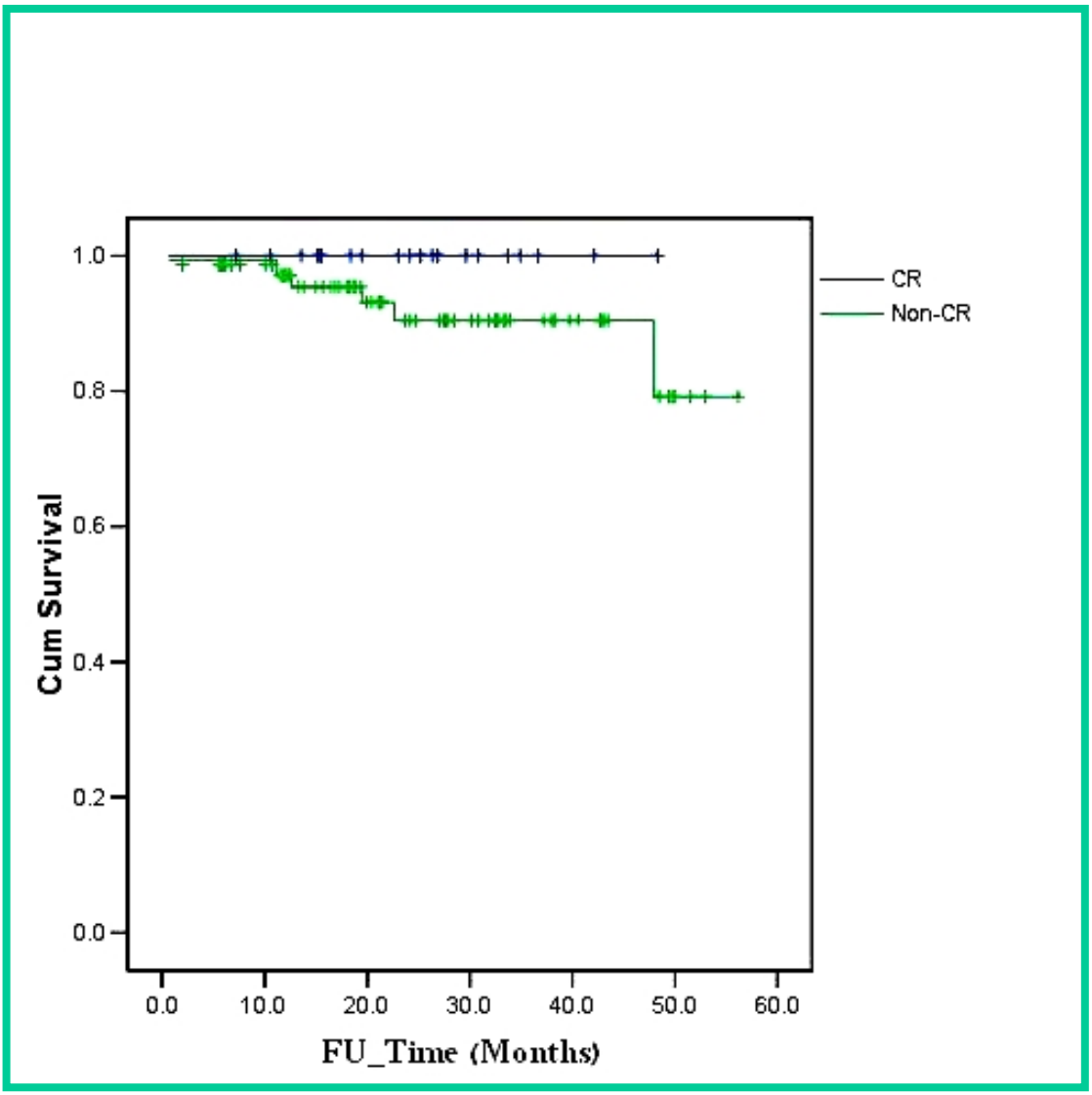
Hagit Tulchinsky, Einat Shmueli, Arie Figer, Ravit Geva, Gideon Goldman, Moshe Inbar, Joseph M. Klausner, Micha Rabau
Department of Surgery B and Oncology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Purpose: To evaluate whether the extent of rectal cancer response to neoadjuvant therapy has an impact on recurrence and survival.
Methods: From 2000 to 2004, 106 patients with locally advanced mid and low rectal cancers were treated with neoadjuvant therapy followed by curative radical surgery with total mesorectal excision. Of them, 96 were followed for a minimum of 6 months and form this study population. Median radiotherapy dose delivered was 50.4 (range 45-50.4) Gy. Ninety patients received 5-fluorouracil-based chemotherapy. The oncologic outcome of patients with pathologic complete response (pCR) and near pCR was examined and compared to that of patients with partial or no response.
Results: Median age was 64 (range, 23-87) years with male predominance (69%). Median distance of the tumor from the anal verge was 5 (range, 1-11) cm. Twenty-two patients (23%) had a pCR or near pCR (19% and 4%, respectively). Patient and tumor characteristics were analyzed and none were associated with pCR. At a median follow up of 23 (range 6-56) months, 17 patients (17.7%) developed disease recurrence. The median time interval between surgery and recurrence was 12 (range 2-56) months. Tumor recurrence according to pathologic response is provided in table 1. Extent of response to neoadjuvant therapy did not have a significant impact on overall survival (p=0.17), (figure1). However, none of the patients with pCR or near pCR had died and only 2 patients developed recurrence.
Conclusions: Our data suggest that pCR and near pCR in response to neoadjuvant therapy are associated with improved local control. Overall survival is probably also positively affected.

Table 1: Disease recurrence

	Non CR (74pts)	**CR (22pts)**	**Total (96pts)**
Local only	7	0	7 (7.3%)
Distant only	6	2	8 (8.3%)
Local +Distance	2	0	2 (2.1%)
Death	6	0	6 (6.3%)
All recurrences	15	2	17 (17.7%)

Figure 1: Overall survival curve (Kaplan-Meier)
Log-rank p=0.17 (NS)



IS TRANSANAL ENDOSCOPIC MICROSURGERY A VALID TREATMENT FOR T2 RECTAL TUMORS?

N. Issa[1], M.M. Krausz[2], S.D. Duek[1]
Colorectal Unit[1], Department of General Surgery A[2], Rambam Medical Center and The Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel

Background: Local excision for T1 rectal cancer with TEM is an accepted standard of care. The role of local excision for the treatment of T2 rectal cancer, however, is far more controversial.
The aim of the present study was to evaluate our results after local excision of T2 rectal cancer using the TEM technique.
Methods: Local excision by TEM was performed in patients with T1 rectal cancer as a curative management, in addition some patients with T2 cancer who were medically unfit, or unwilling to undergo radical surgery with colostomy, or who had a preoperative staging of T1 tumor by the TRUS, were also operated on by the same modality.
Results: Overall, 59 TEM operations for rectal carcinoma were carried out between June 1995 and May 2005. Thirty-eight patients had T1 tumors that were successfully removed with free margins. Twenty-one patients with T2 rectal cancer were operated by TEM; in 16 (76%) of them the tumor was completely removed with clear margins. In 5 patients (23%) with T2 cancer radical surgery was performed following the TEM procedure for positive surgical margins, in 3 of them no cancer was found.
Sixteen patients (76%) had no radical surgery immediately after the TEM, 4 of them disappeared and did not attend regular follow up, but two of them came back after about one year with local recurrence and they were operated.
Twelve patients; 8 refused additional interventions, and 4 were unfit for major surgery underwent adjuvant radiotherapy (external and endocavitary), two of them developed radiation proctitis with rectal bleeding and they were operated.
The 10 other patients had regular follow up (median 3 years) and no local or distant metastasis were found.
Conclusion: Although this study is not a prospective in nature, and the number of patients with T2 cancer is relatively small, the results may support the feasibility of TEM in some T2 rectal tumor. Although the application of TEM combined with radiotherapy appears to be effective in some patients, it should not be considered a standard of care for T2 rectal cancer until new techniques for evaluation of the lymph nodes status will be developed.

ONE-STAGE LAPAROSCOPIC COLORECTAL RESECTION AFTER PLACEMENT OF SELF-EXPANDING METALLIC STENTS FOR COLORECTAL OBSTRUCTION – A PROSPECTIVE STUDY

Mahajna Ahmad[1,3], Wintringer Pascal[1], Beyssac Richard[2], Barbaris Christophe[2], Patrice Talbi[2] , Dulucq Jean-Louis[1]
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Background: The use of endoscopic stents as a bridge to elective one-stage laparoscopic resection in acute colonic obstruction, may prevent urgent surgeries and provide the advantages of two minimally invasive techniques. The aim of this study was to assess a new method of self-expandable metallic stents (SEMS) placement, followed by laparoscopic resection and primary anastomosis for the treatment of acute colonic obstruction

Methods: Fourteen patients, who were diagnosed to have an acute and complete colonic obstruction were treated with endoscopic colonic stenting as a bridge to an elective one-stage laparoscopic resection.

Results: Ninety three percent of technical and clinical success was achieved. The stent insertion related perforation rate was 7% and no other complications were observed. The mean duration of stent insertion was one hour approximately and the mean time between stent insertion and performing the surgery was 6.2 days. Mean operating time was 132 $\pm$ 38 minutes. There were no cases that required conversion to laparotomy and there were no intra-operative complications. One anastomotic leakage was observed. Ambulation time after surgery was 2.8 $\pm$ 0.6 days and length of total hospital stay was 16.4 $\pm$ 5 days. During a period of 11$\pm$ 7 months follow up, neither no recurrences nor port-site metastases were observed.

Conclusion: The management of an acute colonic obstruction by endoscopic stent decompression followed by laparoscopic resection had good results and can be feasible and safe. Larger comparative studies may help in establishing this approach.

REAL TIME-POLYMERASE CHAIN REACTION (PCR) IMPROVES SENSITIVITY OF LYMPHATIC STAGING IN COLON CANCER PATIENTS

Ronit Grinbaum[1], Ali O. Gure[4], Marina Roycetacher[1], Iris Eisenberg[2], Gerd Ritter[4], Lloyd J. Old[4], Herbert R. Freund[1], Tamar Peretz[3], Stella Mitrani-Rosenbaum[2], **Aviram Nissan[1]**
Departments of Surgery[1], Molecular Biology[2], and Oncology[3], Hadassah-Hebrew University Medical Center Mount Scopus, Jerusalem, Israel,
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INTRODUCTION: One third of patients with node negative colorectal cancer (CRC) will ultimately die of disease recurrence within five years of diagnosis. This may be attributable to the inability of conventional histopathologic techniques to identify nodal micrometastasis. The aim of the present study was to develop a reproducible technique of molecular processing of sentinel lymph nodes (SLNs) and to evaluate the added value of Real-time PCR in the detection of micrometastasis in CRC patients.
METHODS: Forty-four SLNs from 35 CRC patients were studied. Enhanced pathologic examination (EPE) including multiple sectioning, H&E and immunohistochemistry staining for cytokeratin was compared to Real-Time PCR for Cytokeratin-20 (**CK-20**) and for a novel molecular marker, **3.6a**. Two lymph nodes obtained from patients without malignant disease and 3 samples of peripheral blood lymphocytes from healthy donors
were used as negative controls.
RESULTS: CK-20 and 3.6a were highly expressed in all 35 primary tumors (positive controls). Of the 44 SLNs, two (4.7%) SLNs were without sufficient RNA for analysis and were excluded from the analysis. All SLNs positive by H&E were also positive by IHC and PCR. Additional 5 SLNs were positive by IHC of which only 2 SLNs were also positive by PCR. Eight additional SLNs negative by EPE were positive by PCR (table 1). None of the 5 negative controls showed amplification of the molecular markers.
CONCLUSION(S): Real-time PCR significantly increases the sensitivity of SLN examination as compared both to H&E and IHC.

Table 1:

Method	n	%positive of all SLNs	Sensitivity	P value
H&E	7/42	16.7%	35%	
IHC	12/42	28.6%	60%	0.001
PCR	17/42	40.5%	85%	0.007
ALL POS	20/42	47.6%	100%	

CROSSLINKED CHITOSAN IMPLANTS AS POTENTIAL DEGRADABLE DEVICES FOR BRACHYTHERAPY: *IN VITRO* AND *IN VIVO* ANALYSIS

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Compared with conventional external beam radiation, brachytherapy offers a superior therapeutic regimen. However, some major constraints are associated with its implementation, including the need for complicated procedures for device placement and removal. The purpose of this study was to examine whether crosslinked chitosan (Ct) implants could serve as potential biodegradable devices for brachytherapy.

Ct was reacted with increasing amounts of glutaraldehyde to obtain hydrogels with different crosslinking densities, which were characterized chemically, thermally and mechanically. The effect of the dialysis medium conditions (ionic strength, osmolarity and pH) on the gel hydration and *in vivo* degradation was assessed. Two types of implants, slow and fast degrading gel (SDG and FDG respectively), were prepared and implanted with or without Sudan Black (SB) in the rat. While SDG withstood for over a month, the FDG degraded within two weeks after implantation. The release kinetics of SB from the hydrogels verified their *in vivo* degradation properties. The incorporation of the radioactive compound ^{131}I-norcholesterol (^{131}I-NC) into the SDG altered the degradation kinetics of the gel as reflected by the release kinetics of the radioactive marker. Eighty percent of ^{131}I-NC was released within a month after implantation, after which time, radioactivity was detected in the regional lymph nodes. It is concluded that hydrogels made of crosslinked Ct are potential novel, degradable devices for brachytherapy.

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ACCURACY OF ENDORECTAL ULTRASOUND IN THE PREOPERATIVE STAGING OF RECTAL ADENOMAS, T1- AND T2-CARCINOMAS

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Background: The aim of this study was to determine the accuracy of endorectal ultrasonography in the preoperative staging of rectal adenomas, T1- and T2-carcinomas. Methods: Between 2/1/1990 and 6/1/2004, a total of 302 patients with rectal adenocarcinoma or adenoma underwent preoperative staging using endorectal ultrasonography at a single institution. The preoperative ultrasound stage was compared with the postoperative histological stage in 122 patients (39 uT0, 36 uT1, and 47 uT2) who underwent surgery with no neoadjuvant chemoradiation. 56 patients underwent radical surgery while 66 underwent transanal excision.

Results: Overall accuracy was 68% in determining the depth of tumor invasion into the rectal wall. Adenomas (uT0) were accurately staged in 87% of cases, while uT1 and uT2 tumors were accurately staged in 61 and 57%, respectively.

	pT0	pT1	pT2	pT3	Total	Accuracy (%)	Understaged (%)	Overstaged (%)	Sensitivity	Specificity
uT0	34	3	1	1	39	87	13		79	94
uT1	6	22	7	1	36	61	22	17	67	85
uT2	3	8	27	9	47	57	19	23	77	77
Total	43	33	35	11	122	68	18	14		

Overall accuracy in predicting nodal spread in the 56 patients who underwent radical surgery was 80% with 14% understaged and 5% overstaged.

Conclusion: These data support previously reported results that endorectal ultrasonography can accurate stage rectal adenomas and can assist in determining individual therapy in patients with benign tumors. The assessment of rectal wall invasion in T1- and T2-carcinomas is less accurate, but may still play a role in clinical decision-making.

BEVACIZUMAB (AVASTIN) BASED NEOADJUVANT THERAPY FOR LIVER METASTASES OF COLORECTAL ORIGIN: AN ISRAELI MULTICENTER COLLABORATIVE STUDY OF THE ISRAELI GASTROINTESTINAL ONCOLOGY GROUP (IGOG)

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As bevacizumab was included in the health basket as neoadjuvant therapy for liver metastases of colorectal origin, it opened a unique opportunity for Israeli oncologists and surgeons to evaluate the clinical and the pathologic response of liver metastases to bevacizumab based therapy.

Patients: 23 consecutive patients, from 4 medical centers, who completed the neoadjuvant therapy and underwent liver metastasectomy are included. Most of the chemotherapy courses employed 4-6 courses of FOLFIRI along with Bevacizumab. CT and PET-CT examinations were conducted before and after the conclusion of the chemotherapy. Each metastasis removed was examined for percent of necrosis and response to therapy.

Results: Mature data is available for 18 patients. The data is presented in table 1. The CT detected **partial response** in 23/33 metastases (69.7%) (RECIST criteria). A complete response per PET-CT was noted in 15/35 metastases (43%), 7 of which showed also pathological CR (7/15 = 46%). Male patients had less chemotherapy courses than female (3.75±0.7 vs 6.5±2.68, $p<0.01$), still 85.7% had a tumor necrosis >70% vs only 14% of the female ($p<0.05$). Necrosis >70% in liver mets was seen in 66.6% of the metastases of elderly >60y compared to only 33% in younger than 60y (p-NS). All 14 metastases (100%) in male patients >60y showed >70% necrosis compared to only 0% (0/7) of metastases of female patients aged >60y ($p<0.05$). The percent necrosis was identical if the metastases were synchronous or metachronous.

Conclusions:

1. Liver metastasectomy can be safely conducted 6 weeks following the last Bevacizumab based chemotherapy course.
2. Only one Bevacizumab related surgical complication was noted (wound dehiscence).
3. 46% (7/15) of the metastases which showed no FDG uptake post chemotherapy, showed a pathological complete remission.
4. Male patients had significantly better pathologic responses than female patients.
5. Synchronous and metachronous metastases have identical response (percent necrosis) to Bevacizumab based therapy.
6. Bevacizumab based neoadjuvant therapy may facilitate liver metastasectomy, far beyond the previously available means.

Table 1

	All	***Male***	***Female***	***p***
Patients	18	8	10	
Age	62±14.8	**67±9.6**	56±16.3	NS
Age range	28-81	55-81	28-76	
No of courses	5.27±2.44	3.75±0.7	**6.5±2.68**	p<0.01
Range of no. of courses	2-12	2-4	4-12	
% patients with CEA reduced	61%	62.5%	60%	
% CT response per patient	55.5%	50%	60%	
% patients with PET CT response	83.3%	87.5%	80%	
% patients with Necrosis>75%	50%	85.7%	14.2%	p<0.05
Median no of metastases	2.44	2.37	2.5	
Median size of mets	3.1±2.05	3.56±2 (18mets)	2.47±2.03 (13mets)	NS
% mets with necrosis >70%	54.5`%	88.8%	13.3%	p<0.05
Time to operation post neoadjuvant	7.37±2.5 weeks	7.14±1.34 weeks	7.5±3.5 weeks	
Age and response				
Age above 60, necrosis >70%	5	5/5 (100%)	0/3	
Age <60, no. of mets with >70% necrosis	2/6 (33%)	1/2	1/4	
Age >60, no. of mets with >70% necrosis	14/21 (66.6%)	14/14 (100%)	0/7 (0%)	p<0.05

LAPAROSCOPIC COLECTOMY FOR COLONIC POLYPS

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Objective: Benign colonic polyps not manageable by colonoscopy, or those with superficial carcinoma, require surgical treatment. Traditionally, formal colectomy with clearance of the lymphatic basin is performed. The aim of this study is to review our experience with the laparoscopic approach for colonic polyps and assess the necessity for radical excision.
Methods: A retrospective chart review of patients who underwent laparoscopic colectomy for colonic polyps was performed. Initial colonoscopic biopsies were compared to the pathology report of the resected specimen.
Results: 49 patients (32 males, 27 females, mean age - 66) underwent laparoscopic colectomy for colonic polyps. Indication for surgery was presumably benign polyp in 38 patients. Superficial carcinoma in polyp was colonoscopically diagnosed in 11 patients. In 7 patients (out of 38) presumably benign lesion harbored cancer diagnosed in the colectomy specimen. None of the 18 patients who eventually had cancer however had any positive lymph nodes.
Conclusions: Although fifth of the presumably benign polyps harbored cancer, none had positive lymph nodes. These preliminary results may question the need for radical lymph node clearance in these patients.

SURGICAL TREATMENT OF COLORECTAL CANCER (CRC) PATIENTS WITH CLINICAL DIAGNOSIS OF HEREDITARY NON POLYPOSIS COLORECTAL CANCER (HNPCC)

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Introduction: HNPCC patients have a 80% lifetime risk for CRC and high incidence of synchronous and metachronous neoplasia. Therefore, once CRC is diagnosed, subtotal colectomy should be considered and the patients should be referred for intensive follow-up.
Aim: To review the surgical procedure performed on our HNPCC patients with CRC and their subsequent follow-up.
Methods: Within our Familial Cancer Clinic (FCC) of 267 pedigrees and 2191 first-degree relatives, we identified 20 patients bearing CRC and fulfilling the clinical (Amsterdam or Bethesda) criteria for HNPCC; 5/20 patients were proven HNPCC mutation carriers.
Results: 10/20 were diagnosed by screening. Median age at diagnosis of primary CRC was 54.6 ±12.3 years. Proximal tumor location was found in 9/20, stage I CRC in 4/20 patients. Synchronous CRC was found in 3/20. Mean follow-up was 7.2±9.8 years, metachronous CRC was eventually found in 2/20; other HNPCC-related tumors developed in 3/20. Subtotal colectomy had been done primarily only in 2/20 of the patients and eventually in one more patient with metachronous CRC.
Conclusion: Only a minority of patients with CRC and clinical diagnosis of HNPCC undergo subtotal colectomy at primary resection. Preoperative consultation with the FCC would facilitate their identification and choosing their optimal surgical procedure and follow-up.

LIGASURE ™ HEMORRHOIDECTOMY - LONG -TERM FOLLOW-UP USING A NEW SCORING METHOD

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Purpose: New techniques of hemorrhoidectomy have been recently introduced in the quest to ease the post-operative convalescence. In 2001 we described a novel method of hemorrhoidal ablation using the Ligasure ™ device. The aim of this study is to evaluate the long-term results of this technique using a new subjective score.

Methods: Between 2000 and 2003 186 patients were operated using the Ligasure device. One hundred and fifty patients (80.6%) were administered a telephone questionnaire using a new scoring method which permits to evaluate quantitatively the efficacy of treatment.

Results: All patients had grade 3 or 4 hemorrhoids. There were 83 males and 67 females, mean age was 49 (range 18 - 80). Mean follow-up was 33.9 months (range 12 - 60). Mean complete post-operative hemorrhoidal score was 1.57 (range 0 - 19, SD 3.4). Late complications: 6 patients (4%) complained of anal stenosis and 27 (18%) suffered of some degree of fecal urgency and occasional incontinence to flatus.

One hundred and eleven patients were very satisfied (74%), 34 patients were satisfied (22.7%) and 5 patients were disappointed (3.3%).

In 52 patients complete pre-operative hemorrhoidal score could be obtained and was compared to the complete post-operative hemorrhoidal score (mean 21.4 [range 8 - 45, SD 6.8] versus mean 1.8 [range 0 - 15, SD 3.4]). This difference was significant ($p<0.0001$).

Conclusions: The Ligasure ™ hemorrhoidectomy is an effective and safe technique with relatively low rate of late complications. Despite late sequelae, patients' overall long-term satisfaction is very high.

RADIOTHERAPY AND CHEMO-RADIOTHERAPY FOR RECTAL CANCER. STATE OF THE ART 2005

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Radiotherapy is well established as an adjunct to surgical resection for rectal adenocarcinoma and has been shown conclusively to improve both local control and survival of patients with rectal cancer. In recent years several of the dilemmas regarding adjuvant radiotherapy such as the timing of radiation (before or after surgery) and the place of radiation for patients undergoing aggressive surgery (such as total mesorectal excision) have been clarified in large prospective randomized studies. The place of chemotherapy in addition to radiation and the choice and schedule of chemotherapeutic agents has become more complicated in recent years with the introduction of newer active agents for advanced colorectal cancer.

Several studies of low rectal cancers have attempted to treat these patients conservatively with chem-radiation and limited surgery.

This review will discuss the indications and choice of treatment protocol for chemo-radiotherapy at all stages of non-metastatic rectal cancer, based on recently reported studies and will discuss the directions of future study in this disease.

MODERN SURGERY FOR RECTAL CANCER

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Cancer is either truly local, or it has already spread elsewhere. In the case of rectal cancer spread is usually to the liver, where it may not be obvious and is termed occult hepatic metastases (OHM).

A patient with occult hepatic metastases will not be cured by local surgery alone. In such a patient, it will not matter whether abdomino-perineal excision or anterior resection is selected; without effective systemic adjuvant treatment the patient will still die. Similarly, the application of radiotherapy, whether preoperatively or postoperatively, will make no difference to the state of the liver, and thus to the patient's ultimate prognosis. Preoperative radiotherapy may make the primary tumour smaller, and in that sense it downstages it, but it makes no difference to any occult metastases in the liver, and so should have very little influence on ultimate survival.

If however the disease is truly local, then adequate local treatment should cure the patient; inadequate local treatment will lead to local recurrence. It follows from the above that surgical endpoints are:

1) Do not kill the patient on the operating table;
2) Avoid local recurrence;
3) Give a good quality of life.

Longer term survival depends either on earlier detection or on the development of effective systemic treatments, neither of which are in the surgeon's control.

The main quality of life issues are the permanent and temporary stoma rate, the frequency and ease of evacuation, and the issues of bladder and sexual function.

Improved technical training should reduce the problems of inadvertent nerve damage. Until clear benefit can be shown for nerve sacrificing operations, they should not regularly be used.

Function of a low rectal anastomosis can be improved by a small colonic reservoir, equivalent in length to one firing of a 55 mm linear stapler. Larger pouches are associated increasingly with reports of evacuation difficulties. It remains to be seen whether over time even the smaller pouches start to have evacuation difficulties. Because of this the elderly seem the optimal group to offer a colonic pouch to, whereas younger patients may still benefit from the straight operation.

Total mesorectal excision (TME) has produced quite heated debate at times. Certainly, surgeons using this technique have remarkably low rates of local recurrence, even in the absence of radiotherapy as an adjuvant. And other surgeons converting to this technique have seen significant improvement in their own figures.

The question at issue is when should TME be applied, and when do the disadvantages outweigh the benefits. TME in many surgeons' hands is synonymous with the use of a temporary defunctioning stoma, whereas standard anterior resection, particularly with higher tumours, often avoids this.

Most surgeons would now accept that TME should be performed for all lower and middle third tumours, and confine the above debate to upper rectal cancer - where perhaps the majority opinion would favour a conventional anterior resection but with a 5 cm clearance of the distal mesentery.

The final issue relates to the use of radiotherapy. Certainly, radiotherapy can make bad results better, but the current question is whether it will improve the very good results achieved by TME or will simply lead to problems.

THE DEXTRAN SULFATE SODIUM (DSS) MOUSE COLITIS MODEL. A MODEL TO STUDY COLITIS ASSOCIATED NEOPLASIA AND ITS CHEMOPREVENTION

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Ulcerative colitis (UC) is associated with an increased risk of colorectal carcinoma. The development of mouse colitis models relevant to human UC are important in order to understand the molecular pathways of carcinogenesis and its chemoprevention. In the Swiss Webster (S-W) mouse DSS induces DALM and flat dysplasias and cancers histologically similar to that in human UC. 15.8% of S-W mice treated with four cycles of DSS developed dysplasia/cancer. The incidence of dysplasia/cancer is significantly associated with levels of inflammation. There is a significant association of nuclear beta-catenin in DALM lesions compared to flat lesions ($p < 0.001$). *Min* mouse have a germline mutation in *Apc* and spontaneously develop colorectal neoplasia. 100% of *Min* mice treated with 2 cycles of DSS develop dysplasia/cancer with a mean number of 29 lesions per mouse which is significantly greater than *Min* mice without DSS ($p < 0.0001$). Dysplasias and cancers are both flat and of the DALM type and loss of *Apc* function is through LOH. 100% of S-W treated with both AOM and DSS develop neoplastic lesions with a mean number of 15.9 lesions per mouse. 62% of $p53^{-/-}$ mice treated with DSS develop neoplastic lesions compared to 20% of $p53^{+/+}$ mice. 50% of the neoplastic lesions in the $p53^{-/-}$ mice are invasive carcinomas compared to 0% in $p53^{+/+}$ mice and 70% of the neoplastic lesions in the $p53^{-/-}$ mice are flat compared to 0% (100% polypoid) in the $p53^{+/+}$ mouse. Celecoxib (300 ppm) reduces the incidence (100% vs 68% - $p = 0.008$) and multiplicity (15.8 vs 7.8 – $p = 0.004$) of colitis associated neoplasia in the AOM/DSS mouse. This reduction of multiplicity is specific for DALMs. Mice treated with Celecoxib had significantly higher inflammation scores than control mice ($p < 0.001$). Celecoxib was not chemopreventive in the *Min*/DSS mouse. 5ASA at a dose of 75 mg/kg significantly reduced the multiplicity of dysplastic lesions in the AOM/DSS model compared to controls (13.8 versus 7.8, $p < 0.05$). This effect was significant for only flat lesions. Inflammation scores were lower ($p = 0.06$) in AOM/DSS mice treated with 5ASA. 5ASA significantly reduced the size of DALM lesions ($p = 0.04$). The DSS Mouse Colitis Model is a good model to study colitis associated neoplasia and its chemoprevention.

THE MEDICO-LEGAL IMPLICATIONS OF CLINICAL GUIDELINES IN COLO-PROCTOLOGY

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Clinical practice guidelines (CPG) are sets of recommendations and algorithms which are systematically developed in order to assist in clinical decision making processes. The two principal medico-legal issues which are associated with CPG are their status as an indicator of the legal standard of care (the reasonable physician test), and whether adherence to them can be used as a defensive argument in medical negligence claims. CPG should be evidence based, and their validity as contemporary standard of care depends on continuous updating. Numerous organizations and panels of experts developed CPG for diseases of the colon and rectum, and the recommendations are often inconsistent and do not represent a consensus. Therefore, the courts should not use CPG as the sole decisive evidence in medical suits. Initially the physicians contested against the doctrine of CPG since they were concerned that it may increase their liability ("sword"), as well as be used by insurers to limit their professional independence. It is widely agreed nowadays that CPG improve the quality of care, and that their developments and implementations by the medical practitioners should be promoted. In order to achieve this goal the physicians must have some legal protection ("shield"). A solution to this problem was tried in Maine, and in several other states, where laws which endorsed CPG, but allow to present them only as a defensive evidence, were enacted. In other words, a plaintiff could not argue that the medical treatment was not in accordance with the CPG, but if the defending practitioner followed the guidelines recommendations he could present it to the court. This approach was criticized since it allegedly contradicts the principle of legal equality and fairness, and in fact it is not clear yet whether it reduced the numbers of negligence claims.

In conclusion: 1. A national CPG system, with continuous updating mechanisms, is a prerequisite before the guidelines would be used as a decisive evidence in medical claims. Until then, the courts would continue to depend on opinions of experts. 2. An efficient legal protection to the medical practitioners is mandatory in order to increase the utilization of CPG.