

tumour cures the patient in more than 90%, provided that no spread has occurred (NO, MO).

The prognosis for TII tumours is not as good (75% cure), and only highly differentiated tumours with no spread as evaluated by MR scanning should be considered possible candidates for local treatment. When resection margins are involved, the tumour is poorly differentiated, and/or vascular or lymphatic invasion has been demonstrated the local treatment should be considered insufficient, and the patient should be offered major surgery immediately. Later major surgery for recurrence (salvage treatment) has a worse prognosis (less than 50% 5 years crude survival).

In patients with severe co-morbidity resulting in a high immediate mortality after major surgery, the above criteria should not be strictly followed, and local treatment, which carries a very low immediate mortality, may be preferred. However, prospective evidence to justify such a policy is scarce.

Adjuvant preoperative radiotherapy may have a place in this context; no large RCT's are available, but selected series have demonstrated 5 years survival up to 75%. It may even be possible to cure some of the rectal cancers by radiotherapy alone.

It has been suggested to give adjuvant chemotherapy for all TII rectal tumours, and high risk TI tumours before or after local excision.

In conclusion, local treatment for early CRC demands a detailed evaluation of stage and clinical status of the patient before embarking on local treatment, and the stage must be revised when the full pathology report is available.

360

### The therapeutic relevance of the molecular biology of colorectal cancer

P.G. Johnston. *Belfast City Hospital Cancer Research Centre, Department of Oncology, Belfast, N. Ireland*

**Introduction:** The fluoropyrimidine 5-Fluorouracil (5-FU) is widely used in the treatment of colorectal cancer. Fluoropyrimidines were developed in the 1950s following the observation that rat hepatomas utilized uracil more rapidly than normal tissues, suggesting that uracil metabolism was a potential target for antimetabolite chemotherapy. The mechanism of 5-FU cytotoxicity has been ascribed to the misincorporation of fluoronucleotides into RNA and DNA and to the inhibition of the nucleotide synthetic enzyme thymidylate synthase (TS). While 5-FU in combination with other chemotherapeutic agents improves response rates and survival in breast and head and neck cancers, it is in colorectal cancer that 5-FU has had the greatest impact. It has been demonstrated that 5-FU-based chemotherapy improves overall survival and disease-free survival of patients with resected stage III colorectal cancer. Nonetheless, in the metastatic disease setting, response rates for 5-FU-based chemotherapy as a first-line treatment for advanced colorectal cancer are only 10-20%. Combination of 5-FU with the newer chemotherapies - irinotecan (CPT-11) and oxaliplatin - has improved the response rates of advanced colorectal cancer to 40-50%. However, despite these improvements, new therapeutic strategies are urgently needed. DNA microarray technology has the potential to identify novel genes that may play key roles in mediating resistance to 5-FU-based chemotherapy. Such genes may be therapeutically valuable as predictive biomarkers of 5-FU chemosensitivity and/or provide new molecular targets that overcome drug resistance. This talk reviews how pre-clinical and clinical studies have impacted on the clinical use of 5-FU and discusses how DNA microarray profiling may affect its future clinical application.

361

### Surgery - radiotherapy: when and how to combine?

L. Pahlman. *University Hospital Uppsala, Department of Surgery, Uppsala, Sweden*

According to meta-analyses covering all randomised trials it is obvious that the best reduction in local recurrences is received if radiotherapy is given preoperatively. In the postoperative setting similar data can be achieved if radiotherapy is combined with chemotherapy. Moreover, data do support that preop radiotherapy is superior to postoperative treatment.

The problem with the preoperative approach is the drawback of treating too many patients in vain. Therefore, good staging is necessary. Based upon the data from all studies, low rectal cancer, tumours growing anteriorly, narrow male pelvis, and obese patients are at risk. Also stage of disease is important to find preoperatively. The problem with this risk analysis is the fact that all data are from trials using "old fashion" surgery. With a more appropriate surgical technique, i.e., the use of TME (Total Mesorectal Excision), the risk calculations might be changed.

When taking staging into consideration it is important to focus on where part in the multimodal treatment, which is the "weak" one. Also it is important to identify situations when a combined treatment is superfluous. The "weak" part is the way the surgeon can make a curative loco-regional procedure and the best prognostic factor is the circumferential margin. The local only imaging technique picking up the circumferential margin with a high sensitivity is modern MRI staging. Based upon good MRI imaging it is possible to divide the patients with a rectal cancer into three groups; good, bad and ugly. The good cases have a wide circumferential margin and need no radiotherapy. The bad one has a narrow circumferential margin and would certainly benefit from preoperative radiotherapy. The ugly looking group has a positive circumferential margin. Those patients will probably do best if preoperative radiotherapy is combined with chemotherapy.

**Conclusion:** Radiotherapy should be used selectively based upon the preoperative imaging of the tumour size. In this staging not only the T-stage but also the N-stage is important in terms of identifying the distance to the circumferential margin when the specimen has been retrieved after high quality TME surgery.

362

### Chemoprevention - a realistic option

Abstract not received.

363

### Social inequality and risk of cancer - do we have a problem?

K. Lillberg<sup>1,2</sup>. <sup>1</sup> *University of Helsinki, Department of Public Health Helsinki, Finland;* <sup>2</sup> *University of Turku, Department of Public Health, Turku, Finland*

Socio-economic status is known to be associated with the risk of many cancers, though limited data are available on potential variation in these associations between countries and over time within countries. Possible factors responsible for socio-economic differences in cancer risk include lifestyle factors (e.g., smoking, diet, reproductive factors and sexual behaviour), work and living environment, and access to health care services.

In large population-based studies on social class and cancer risk among working-aged Finns during 1971-1985/95 (e.g., [1,2]), the cancers found to be associated with low social class included, e.g., those of the lip, oesophagus, stomach, larynx, cervix uteri and lung (the latter only in men). Cancers of the colon, prostate and breast, and skin melanoma in the trunk and limbs were most common in high social classes. In some cancers the positive social class gradients diminished (e.g., testicular cancer) or disappeared (e.g., cancer of the corpus uteri) during the observation period; the positive gradient seen in female lung cancer in the 1970s reversed to a negative one in the 1980s. Most of the observed patterns can be at least partially explained by the social class distribution of the known risk factors for cancers in Finland. Overall, it was estimated that about 26% of all cancer cases among working-aged Finns during 1971-85 could have been avoided if all social classes had been able to maintain a lifestyle similar to that of the social class with the lowest incidence.

In conclusion, known risk factors for cancer, particularly smoking, appear to account for a substantial proportion of the socio-economic differences in cancer risk, but unknown factors are likely to contribute as well. A current challenge for epidemiologists is thus to uncover what is still hidden behind the socio-economic differences in the risk of certain cancers; that for policy makers and health care practitioners is to continue the fight against smoking and other unhealthy behaviour and to reduce social inequalities (where such exist) in access to health care services.

### References

- [1] Pukkala E, Weiderpass E. Time trends in socio-economic differences in incidence rates of cancers of the breast and female genital organs (Finland, 1971-95). *Int J Cancer* 1999;81:56-61.
- [2] Pukkala E, Weiderpass E. Socio-economic differences in incidence rates of cancers of the male genital organs in Finland, 1971-95. *Int J Cancer* 2002;102:643-8.