CANCER OF THE COLON AND RECTUM

THE SEVENTH KING'S FUND FORUM

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Consensus Statement

In London from 18-20 June
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The panel comprised:

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Consensus Statement

Last year, 22,000 people died of cancer of the colon and rectum in Britain and of those diagnosed this year less than 30% will survive 5 years. Cancer of the colon and rectum is the second most frequent cause of cancer death in Britain and the Western World. In the past 20 years, treatment has had little impact on the survival. It is a disease mainly of older people, and the numbers of new cases and deaths will continue to increase with the growing numbers of the elderly. There is little public recognition of the fact that in Britain today there may be over a quarter of a million people living with cancer of the large bowel. This may partly be due to the stigma and embarrassment of bowel cancer. Some patients delay seeking help through fear and ignorance. Others require major emergency surgery for which they are totally unprepared. Knowledge about this cancer has remained rather more in the medical domain than some others such as breast cancer. For this reason it is hoped that our consensus statement will raise public awareness of this common and often devastating disease.

The panel was asked to address the following questions:

1. **Would the detection and treatment of polyps reduce the incidence of cancer of the colon and rectum?**

2. **Are there other preventative measures which will safely reduce the incidence and mortality of cancer of the colon and rectum?**
3. **How effective are current treatments for cancer of the colon and rectum at improving survival and quality of life?**

4. **What is the direction for future research?**

Throughout the statement specific recommendations have been highlighted in italics.

1. Would the detection and treatment of polyps reduce the incidence of cancer of the colon and rectum?

It is important to define a number of terms before discussing particular questions of prevention and management. Most polyps and all colorectal cancers are neoplasms or new growths. Cancer is diagnosed histologically when the growth invades locally through the inner lining of the bowel. A more precise term for a neoplastic polyp is an adenoma. Three types of adenoma can be defined by the pathologist: tubular, tubulo-villous and villous, of which the latter is thought to have the greatest invasive potential.

Whether or not the detection of polyps would reduce the incidence of cancer of the colon and rectum depends upon the premise that most colorectal cancers develop from adenomatous polyps. There is now a great deal of circumstantial evidence to support this, although alternative mechanisms may account for the carcinomas which arise in patients with longstanding ulcerative colitis and the rare cancers which arise apparently *de novo*.

When the adenoma-carcinoma sequence was first proposed the evidence came from epidemiological and clinical studies alone. For example, in countries with a low prevalence of adenomas the incidence of colorectal carcinoma is also low. Studies of patients with the genetic condition familial adenomatous polyposis (FAP, formerly known as Gardners Syndrome or polyposis coli), where affected individuals have multiple large bowel tubular adenomas and a high risk of colorectal cancer, support this hypothesis. Recent molecular genetic studies have added strong evidence for the concept of the adenoma-carcinoma sequence.

If the great majority of cancers develop within an adenoma, it follows that detection and removal of polyps in asymptomatic individuals should theoretically reduce cancer incidence and mortality. The problem is that autopsy studies have shown adenomas to be far more prevalent than carcinomas (30% compared to 2%). Double contrast barium enema may be used to diagnose polyps, but the most reliable diagnostic technique for the detection of adenomas is colonoscopy. However, it is invasive and there are no good colonoscopic indicators of malignant potential other than size. *There is therefore no case for colonoscopic screening on a population basis.*

Evidence from occult blood screening of asymptomatic populations suggests that it may detect the larger and more friable adenomas with a higher risk of malignant change, but at present no judgement can be made on whether this confers survival benefit. The results of the European randomized controlled trials for screening will consider this question and may provide evidence as to whether the smaller adenoma detected by the screening method presents as a cancer at a later screening round or as an interval cancer (ie presenting between screening rounds).

We recommend that the use of colonoscopy in the asymptomatic individual is justified only in those with a high genetic risk of developing cancer and in the follow-up of some of those patients who have had a symptomatic adenoma previously removed endoscopically.

We recommend that in the symptomatic patient with a polyp the whole of the large bowel is examined and polyps greater than 5mm in diameter removed. The management of polyps less than 5 mm is a problem which will be resolved only by more studies of their natural history.

It is uncertain which patients require follow up after removal of symptomatic polyps and how often. Development of new (metachronous) adenomas is variable and information regarding this comes mainly from retrospective surgical, and only a limited number of prospective endoscopic, studies. *Follow-up is not indicated for patients with a single small tubular rectal adenoma and those over the age of 75. Those individuals with a large adenoma or any type of multiple adenomas should undergo colonoscopic surveillance at 3-5 yearly intervals.* The risks of colonoscopy are small but real and can be minimised by an expert colonoscopist.

We recommend that in order to deal adequately with the existing demands of symptomatic individuals and screening of high risk groups, provision for colonoscopic services, including training, need to be improved.

2. What preventative measures are there which will safely reduce the incidence and mortality of cancer of the colon and rectum?

Reduction in incidence and mortality may be achieved by reducing exposure to causative factors eg diet or by detecting the condition at a pre-malignant stage through screening.

Diet

The wide geographical variations in colorectal cancer incidence which exist suggest a strong environmental influence and this is confirmed by studies of migrant groups. Interest in dietary aetiology began with the hypothesis that the higher fibre intake of low incidence populations protected them against colorectal cancer. There are great methodological difficulties in studying the association between diet and cancer. Most of the epidemiological evidence is weak, based mainly on correlations at a population level and a small number of case-control studies. It is necessary to be cautious about generalising from animal studies.

A dietary aetiology is plausible because diet has been shown to have an important influence on bowel function and metabolism. So far, the main factors linked with increased colorectal cancer have been high intakes of fat and energy, and low intakes of fruit and vegetable fibre. Cereal fibre does not appear to provide any protection against colorectal cancer.

Although there is a general view that diet is probably the most important environmental cause of colorectal cancer *the evidence is not strong enough to recommend dietary changes*. However, a reduction in fat and energy intake and an increase in fruit and vegetable fibre would be in line with recommendations for dietary change relating to other diseases.

Screening

It has been suggested that screening may decrease morbidity and mortality of colorectal cancer by the detection of early cancers in high risk groups and the population.

Population screening

Rectal examination, sigmoidoscopy and faecal occult blood (FOB) testing have all been suggested as methods of screening asymptomatic populations. The first two are impracticable as screening tools and would detect only a small proportion of distal cancers. Faecal occult blood testing (eg Haemoccult) is non-invasive but has problems of limited specificity and sensitivity and is taken up by around 60% of those offered it.

Because of various biases the efficacy of screening must be evaluated by randomised controlled trials (RCTs) using population mortality and other outcome measures.

Results from RCTs suggest that cancers detected in the screened population are more likely to be at an early stage than cancers presenting in an unscreened population, and that a higher proportion can be dealt with endoscopically rather than surgically. However we do not yet know whether screening will significantly improve the duration or quality of life in a population offered screening compared with a population not offered screening. Any decision on a screening programme must take account of all the costs including the foregone benefits of displaced alternative projects. In addition to the effects on NHS and other public sector costs, the costs to patients and their families must be considered including the unnecessary anxiety and the risks of complications of colonoscopy for false positives. In the event that screening is introduced, it will be necessary to ensure that there are additional diagnostic facilities available to meet the demand for additional tests generated by the programme. It will also be important that people offered screening are told about the implications of the different outcomes of the tests. A large study of FOB screening is currently in progress in Nottingham and its results are expected in 1995. *We recommend that no decision on the introduction of FOB population screening is made before 1995.*

Screening of high risk groups

In individuals with a high genetic risk of developing adenomas/ carcinomas the balance of benefits of screening in relation to risks and costs is more favourable than for the general population. Response and detection rates are improved and invasive procedures may be justified.

Those at highest genetic risk are the offspring of individuals with FAP and the two hereditary non-polyposis colorectal cancer (HNPCC) syndromes. These conditions are autosomal dominantly inherited and are estimated to account for 0.5-1% and 5-10% of all colorectal cancers respectively. The diagnosis of FAP is straightforward although clinicians should be aware that 30% of people presenting may have no family history. The clinician should be alerted to the possibility of the HNPCC syndromes by the occurrence of colorectal cancer in young people and particularly where the lesion is rightsided. Affected relatives may be identified in the family with either colorectal disease or adenocarcinoma elsewhere (eg of breast, uterus, ovary).

There is a significant increased frequency of colorectal cancer in first degree relatives of people with colorectal cancer. The empiric risk of developing cancer varies from 1:17 for individuals with one first degree relative affected to 1:6 with two first degree relatives. *We recommend that a comprehensive family history is taken as part of the assessment of all individuals with colorectal cancer.*

Those families in which a significant genetic risk is suspected should be referred for genetic counselling and accurate risk determination. *We recommend that, given the number of people involved and the resource consequences, such screening must be evaluated.*

Recent advances in molecular biology mean that there is the potential to use linked DNA markers in FAP families to determine genetic risk, thus confining the need for regular colonoscopic surveillance to those family members at high risk. Markers for other dominant syndromes may be available in the near future.

Case finding

This is the identification of affected but asymptomatic individuals by opportunistic screening eg when a patient presents to the GP with an unrelated condition. In the absence of an adequately evaluated non-invasive screening method, case finding cannot be recommended. However, the taking of a good family history is essential as it may identify a high risk individual who should be referred for further investigation.

Assessment of the symptomatic patient

Patients with colorectal cancers usually present to their general practitioner with non-specific gastrointestinal symptoms. Delay in referral and diagnosis may influence outcome. Abdominal and rectal examinations are essential to determine the urgency of referral. There is evidence that they are not carried out on a large proportion of patients who are subsequently found to have colorectal cancer. *FOB testing is of no value in the assessment of the symptomatic patient in general practice because of its low specificity and sensitivity.*

3. How effective are current treatments for cancer of the colon and rectum at improving survival and quality of life?

The efficacy of treatment is limited. Survival and quality of life after treatment for colorectal cancer will vary according to the individual patient, the site and stage of the tumour, its presentation, its treatment as an emergency or an elective case, and between hospitals. Increasingly, treatment involves a number of disciplines and a team approach is essential.

Surgery

Most patients referred to hospital will first be seen by a surgeon. There is good evidence that variations in operative mortality, post-operative morbidity, and survival are all surgeon related. The skill and training of the operating surgeon has a crucial effect on outcome. This particularly applies to rectal surgery, in which major procedures carry a significant risk of damage to nerves supplying the bladder and sexual organs. There is no formal organisation for colorectal surgery in the UK, and it is not yet recognised as a separate sub-specialty. The newly formed Association of Colorectal Surgeons of Great Britain and Ireland should assist in this development. *We recommend that each district should have at least one colorectal surgeon* or, failing this, colorectal cancer patients should be referred to another hospital which does have a specialist. Even then local surgeons should be organised so that one can assume responsibility for colorectal cancer. *Proper local referral and treatment protocols should be developed for both elective and emergency colorectal surgery.*

Advanced surgical techniques, encouraged by specialisation, have reduced the need for a permanent colostomy, but despite this increasing trend some patients are treated with a colostomy unnecessarily. Tumours close to the anal canal still have to be treated by excision of the rectum and a colostomy. *Those patients who do require a temporary or permanent colostomy will continue to need the support of specialist stoma nurses.* Adequate resources must be properly provided. Their extended role will include both information on new appliances and techniques, and counselling before and after surgery.

Pathology

The accurate reporting of histopathology on resection and polypectomy specimens is time consuming but essential for the assessment of prognosis and further treatment. *Standards of reporting have recently been outlined by the United Kingdom Central Committee for Cancer Research (UKCCCR) and should be adhered to.* Adequate support, staff and resources must be provided for this important task.

Radiotherapy

For rectal cancer preoperative radiotherapy reduces the incidence of local recurrence, but some early cancers may be treated unnecessarily.

Similar benefit accrues from radiotherapy given postoperatively which permits the selection of those patients with later stage disease. There is however a greater risk of side effects. Although radiotherapy helps to prevent recurrence there is no evidence that it prolongs survival. Palliative radiotherapy may also have a useful role to play in patients with established disease particularly in the pelvis.

Chemotherapy

Adjuvant chemotherapy (that is, given at the time of surgery) aims to control the metastatic potential of a tumour. Up to 25% of patients with colorectal cancer develop liver metastases. The recently introduced AXIS national trial of adjuvant chemotherapy and radiotherapy is assessing the effect of 5 fluoro-uracil (5FU) infusion into the portal vein. *We recommend that surgeons enter suitable patients into the AXIS national trial.*

Recent evidence suggests that patients with advanced (Stage C) colon tumours may be improved by adjuvant therapy with 5FU and levamisole, and such patients not entered into trials should be considered for this treatment.

Studies in advanced colorectal cancer treated with 5FU and folinic acid show some value and may be effective as palliation in patients with advanced disease.

Other palliative treatments

Older patients who are frail and might otherwise have a colostomy or major resection with a high mortality can be treated by laser therapy or transanal resection to reduce distressing symptoms. In carefully selected cases, partial liver resections for one or two metastases confined to a single lobe of the liver may prolong survival and offer useful palliation. General palliative care is crucially important as with other cancers.

Follow-up

Arrangements for follow-up in the UK are haphazard and poorly organised. The aims of follow-up are the detection of overlooked synchronous tumours, the detection of recurrent cancer and new tumours at an early stage, patient support, and the audit of results. *Follow-up is expensive and studies of its efficacy, organisation, frequency and new methods of detection are needed.* For example, the use of the tumour marker CEA (Carcino Embryonic Antigen) as an indicator of local recurrence is being assessed, and optimal post operative colonoscopy screening intervals need to be determined. Colorectal specialisation would encourage the inclusion of patients in trials with systematic follow up protocols.

Measuring outcome

The standard medical assessment of outcome that concentrates on survival, disease free interval and recurrence may under or over estimate the benefit of treatment. Patients however are extremely concerned about the quality not just the quantity of life. Valid standardised tests of quality of life which assess the impact of treatment on psychological, social, occupational and sexual functioning are available and have proved useful in the treatment of other types of cancer. *These tests have not been used in trials of colorectal cancer therapy, and must be used routinely in the future.*

Better information

There is widespread ignorance about colorectal anatomy, function, disease and treatment. Good information about services, treatment outcomes and quality of care is essential if patients are to be able to

make informed choices. The full range of cancer information agencies have an important part to play here. As quality assurance prompts hospitals to publish results of treatments and outcomes, patients and their general practitioners will begin to change referral patterns which could reinforce specialisation. *It is critical that measures of outcome are properly audited, and made available to the general public.*

Regional cancer registries provide invaluable information and should be supported.

4. What is the direction for future research?

Research

There are gaps in our knowledge about the natural history of colorectal cancer and the effects of treatment. At present only 2% of colorectal cancer patients are entered into clinical trials. The resource implications of new screening or treatment approaches must be carefully considered. *In addition to those areas highlighted already we wish to recommend that research efforts be directed towards the following:*

1. *The natural history of the adenoma, dysplasia and cancer, and the effects of intervention.*

2. *The molecular biology of colorectal cancer.*

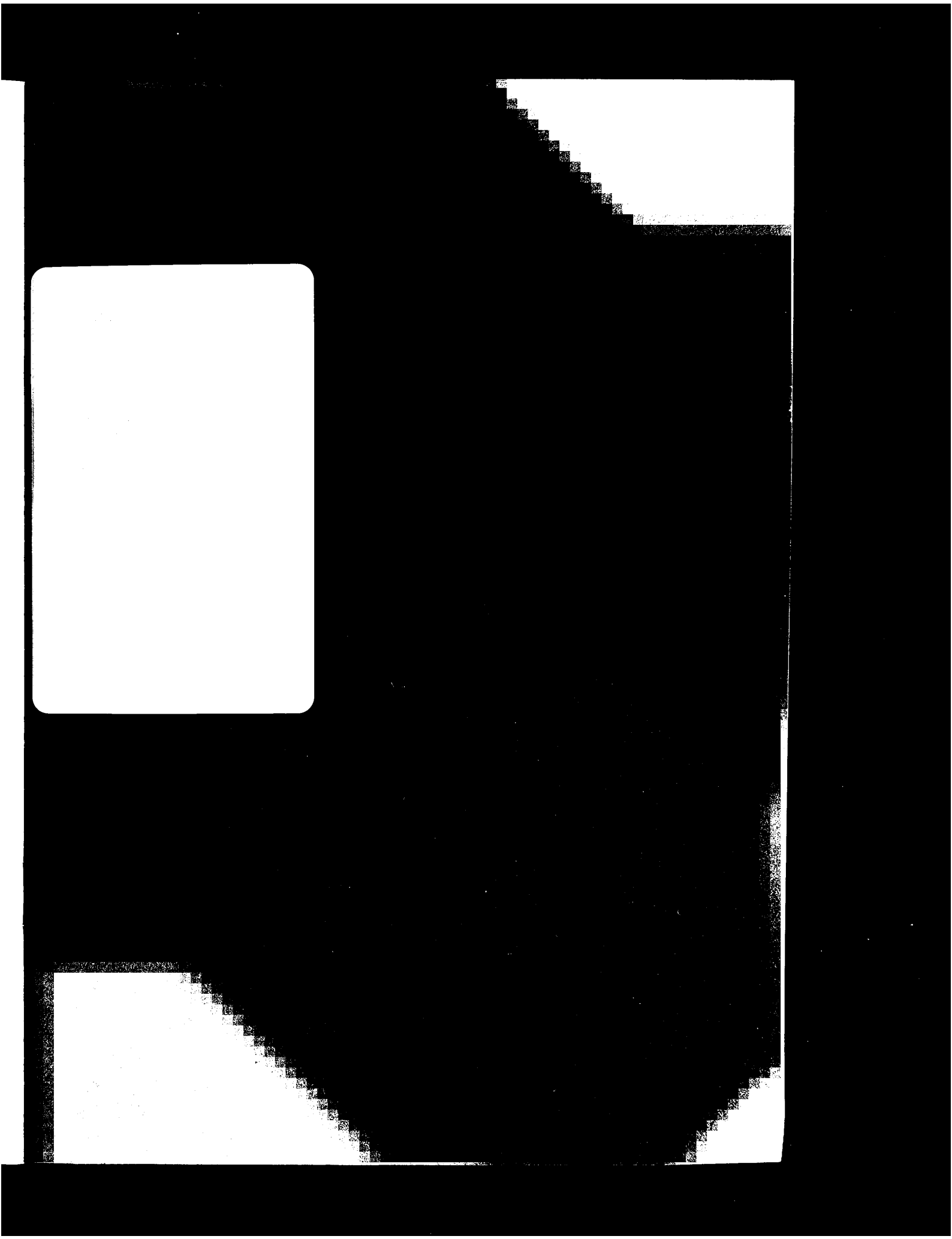
3. *Hereditary factors - the evaluation of the practical and social implications of surveillance of high risk families.*

4. *The development of more sensitive tests of the physical and biological activity of tumours in order to facilitate the accurate pre and post operative staging of colorectal cancer.*

5. *The development of new treatments to improve survival and quality of life.*

6. *The use of validated quality of life measures in all clinical trials of colorectal cancer therapy.*

7. *Studies which will provide insights into the patients' experience of colorectal cancer, its treatment and the impact on their lives.*



One copy of the consensus statement is available free of charge on request from:

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