KING's FUND CENTRE

Cancer of the Colon and the Rectum

a guide to the issues and controversies

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June 1990

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INTRODUCTION

This booklet has been produced for members of the audience of the Kings Fund Forum on Cancer of the Colon and Rectum. It aims to provide a simple introduction to the subject and an explanation of some of the concepts and terms which will be used through out this conference.

Cancer of the colon and rectum is the second most frequent cause of cancer death in Britain and the Western World. 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. In the last 20 years treatment has had little impact on the survival. It is a disease primarily of older people, and the numbers of new cases and deaths from cancer of the large bowel will continue to increase in parallel with the growing numbers of the elderly. There has been little public recognition of the fact that in Britain today there are over a quarter of a million people living with cancer of the large bowel.This may partly be due to the stigma of cancer but is also likely to be a symptom of the embarrassment which often surrounds the bowel. Lack of public knowledge has resulted in this cancer remaining rather more in the medical domain than others such as breast cancer. For this reason it is hoped that this conference will raise public awareness of this common and often devastating disease.

The first section of the booklet explains the scale of the problem in terms of the natural history of the disease and how the disease is thought to develop. Section two discusses the genetic and environmental influences which may cause this disease and highlights the main areas of debate. Section three reviews the principles of prevention and focuses particularly on the issues and controversies around screening. Section four looks at aspects of treatment.

Terminology

Cancer of the colon and rectum is known by other names which include colorectal cancer, (large) bowel cancer or intestinal cancer. The two cancers are often discussed together because of their similarity.

SECTION 1

The Scale of the problem

Every year more than 20000 people die from cancer of the colon and the rectum in Britain. Lung cancer alone accounts for most cancer deaths whereas breast cancer which has such prominence accounts for 13000 deaths the vast majority occurring in women.

The data source of information on new cases of cancer treatment and survival in most countries are the cancer registries (a voluntary notification by doctors in Britain). The death rates when standardised for age and sex have shown no improvement over the last 2 decades in spite of progress in treatment. The overall survival is still less than 27% overall. The younger the person and the earlier the tumour presents the better is the survival.

Death rates and survival vary both internationally and nationally, These may partly be explained by case ascertainment and registration but may also reflect differences in health care. The gravity of this cancer is reflected not only in Europe but in the U.S.A. Last year there were 150000 new cases of this condition in America and a similar number in Europe. In Britain the life time risk of cancer of the colon is 1 in 50 for men and 1 in 40 for women. For cancer of the rectum is 1 in 62 for men and 1 in 74 for women.

How does it develop?.

The theory of how colorectal cancer develops is based on two observations. Just as large bowel cancer is rare in rural Africa, so too is the occurrence of a condition called intestinal polyps. This is in contrast to the Western World where intestinal polyps are extremely common in the population, and like large bowel cancer, increase with age. The other observation was that a rare inherited form of disease, familial adenomatous polyposis (F.A.P.) could provide a useful model for cancer. The observation that in this disease cancer first started in polyps led to the development of the 'polyp- cancer sequence' theory.

The polyp cancer sequence

What is a polyp?

A polyp is a piece of tissue forming a lump on the inside of the bowel. Polyps differ in size and type. Some are flat, others raised, others may be on stalks. Polyps tend to occur multiply and are thought to disappear and reappear throughout a persons life. As well as differing in external appearance and size they differ in internal structure. The study of internal architecture is called histology.

It is now believed that although some cancers can arise spontaneously from the normal bowel tissue the vast majority arise from the polyp. However only a very small proportion of polyps become cancerous since many more people have polyps than cancer. For instance in the population over 60 years as many as many as 6 people out of 10 will have polyps whereas the number of people with colorectal cancer is less than 3 in a thousand. And so a major problem is determining which polyps will become malignant.

Which polyps become cancer?

There are two main predictors of malignancy. The first is size, where the risk of malignancy increases with increasing size. The other feature is the histology or internal architecture. The group of polyps which are most likely to become malignant are called villous adenomatous polyps . This type of polyp accounts for only 10% of all the polyps occurring in the large bowel and of these less than half will actually become malignant. It also seems that most polyps are very slow growing and it may take 10-30 years for a polyp to become a cancer. Similarly, even if a polyp does become a cancer, the cancer itself may be slow growing and take a number of years to manifest clinically. Unfortunately until the polyp has been surgically removed and looked at under the microscope it is impossible to determine its type. This means that as many as 25 polyps may have to be removed to prevent one possible cancer and some people will have polyps removed unnecessarily. The removal of polyps

is a surgical procedure and not without its own risks. As a result there are a number of unanswered questions and difficult decisions for the patient and the doctor.

These are some of the questions which may be raised through out the conference.

* Is it possible to predict without removing polyps those with malignant potential?

* How long does it take for the polyp to become a cancer?

* What is the true lifetime risk of an individual with polyps developing cancer?

* How many polyps have to be removed to prevent one cancer?

* How many people die with polyps or cancers which are not discovered in their life time?

* What is the risk of removing polyps compared to the risk of leaving them alone?

It is particularly important to understand these issues as they form part of the current debate surrounding not only prevention but also treatment.

Staging a cancer

When a cancer develops it is convenient to define whether the cancer is still confined locally or has spread: this is known as staging. Doctors have developed staging systems for all cancers. Cancer of the colon and rectum has a modified system named after the pathologist who first described it," Dukes", Over the years a number of other systems have been developed with different criteria in an attempt to predict the future course of the disease (prognosis) Staging is important because it helps the clinician to determine the appropriate treatment and at present it is the only useful indicator of prognosis. Whether a cancer develops from normal tissue or from a polyp the same staging criteria apply.

Dukes Stage A - is when the cancer is confined locally to the bowel.

Dukes Stage B - is when the tumour has spread through the bowel wall

Dukes Stage C - the cancer has spread to involve the lymph nodes

Dukes Stage D - distant spread of tumour to other organs in the body most commonly the liver.

Throughout this conference other staging systems may be referred to but the principles are the same , namely to develop a good method so that treatments can be compared in patients. It is still unknown how long it takes for a cancer to go through the various stages and it is likely that different cancers behave in different ways so that some may be slowly growing over many years whereas others may grow rapidly over months.

Who gets it?

Cancer of the large bowel is a cancer of the Western world ; it is rare in underdeveloped countries. Studies of people who have come to the West show that the risk of getting cancer increases over their lifetime to that of the country they move to. There are three main groups of people in the population who are at risk of developing colorectal cancer.

i. By far the greatest number of cancers arise in the population where there is no identifiable risk factor. In this group it seems that age is the single determinant of cancer. It is rare under the age of 40 years but the incidence of colorectal cancer doubles every decade after the age of 40 years and it follows that the risk parallels this increase. Although there is no difference between the sexes , more women get cancer simply on account of the population structure.

ii. The second group of people who are at risk of developing cancer is those with two or more first degree relatives who have had a cancer of the colon, rectum, breast or uterus. This is called the family cancer syndrome . There are some other conditions such as inflammatory bowel disease which may predispose the individual to cancer. This whole group accounts for less than 10% of all the cancers of the large bowel.

iii. The last group are those who have a rare form of inherited disease called familial adenomatous polyposis. This is a condition where there are thousands of tiny polyps in the bowel which have the potential for malignancy. This condition is inherited as a dominant gene which means that an individual will have a 50:50 chance of inheriting the disease from an affected parent. Most of the deaths occurring under the age of 40 are due to this condition.However this form of cancer accounts for less than 1 % of all the cases of cancer of the large bowel in the population.

SECTION TWO.

What causes it

The current theory is that genetics and the environment interact to cause most of the common types of bowel cancer, but in the rare forms genetics may play the larger role.

1. Genetic factors

The evidence for a genetic cause of cancer is based on the previously mentioned observations that patients with familial adenomatous polyposis coli inevitably develop cancer of the colon or the rectum and that people have an increased risk of bowel cancer if 2 or more members of their family have cancer of the bowel, breast or uterus. Since blood relatives are affected rather than spouses it is unlikely that the influence is purely environmental. Geneticists have studied the chromosomes where the responsible genes are located and have been able to find some of the genes responsible. This has now prompted workers to see whether the same thing can be done in the general population who have no readily identifiable risk of cancer. It seems that there may be a genetic technique available in the future to detect those at risk of cancer. This has implications for the future detection and prevention of disease.

2. Environmental factors

Compared to the Western World, in rural Africa cancer of the large bowel is a rare disease, resulting in speculation that dietary factors may play an important part in causing disease. Some of the factors that have recently been looked at include starch, fibre, animal fat and vitamins. The evidence is still not strong enough to say which factors, if any, are the most important. For those interested there is a good review of the dietary evidence for cancer which has been published by the Health Education Authority. Diet is only one of a number of environmental factors that have been implicated in cancer : others include beer consumption, particular occupations and lower social class.

SECTION THREE

Prevention

For convenience it is easiest to consider prevention under three main categories; primary, secondary and tertiary.

Primary prevention

Primary prevention has as it aim a reduction in the number of new cases of disease occurring over a period of time(incidence). An example of this is vaccination against infectious disease or preventing lung cancer by not smoking cigarettes. Thus primary prevention primarily addresses the cause. But for cancer of the colon and rectum the cause remains uncertain and so there is not yet an effective intervention strategy which will prevent the disease.

Secondary prevention

Where there is no cure or preventable measure for a disease attention turns to secondary prevention. Secondary Prevention aims to reduce the number of cases of the disease occurring at a given time(prevalence) and therefore the mortality from the disease. Thus strategies rely on detecting the disease at an early stage in order to instigate curative treatment. There are various methods of prevention but the two methods currently in use for colorectal cancer are case finding and screening.

i) Case Finding

Case finding for colorectal cancer identifies the high risk person either opportunistically when the individual lands up in a clinic or through tracing relatives of affected individuals. This involves setting up a register of families. This group of people belongs either to the FAP or family cancer group. Case finding may not be efficient as total coverage of the population is not possible. Many of the dilemmas faced are covered in the screening section but some of the questions include:

* What percentage of people in the population belong to the high risk groups above?

* How can this group be identified efficiently?

* What are the costs and benefits of case finding and what evaluation has been undertaken?

ii) Screening

Screening involves identifying a group from the general population at high risk of developing cancer who then undergo an appropriate diagnostic test for cancer. Screening programmes can not predict the individual who will gain but the benefit is for the population and hence this is called a population approach. Over the years people have been developing tests in an effort to detect early cancer.

There is not yet a genetic technique (probe) to screen the population and to date the only test available for screening for colorectal cancer is the faecal occult blood test.

Screening for colorectal cancer

Members of the audience may have already seen some of the cancer research campaign advertisements for research into Magic toilet paper. This is a research campaign for screening for colorectal cancer based on the faecal occult blood test.

In Britain there is currently no formally recommended screening programme for colorectal cancer because the benefits of screening are still unclear. At present there are 3 randomised trials of screening currently in progress in Europe to assess whether it is worth screening for this condition. In these trials a large population is selected and randomly allocated to one of two groups. The first group is the group which is actively screened and the second group has no active intervention.

Faecal Occult Blood Test.

This test is based on the premise that bowel cancers have an increased tendency to bleed. A specially treated strip of paper changes colour when it is in contact with blood and is capable of detecting in the faeces tiny traces of blood invisible to the naked eye. The test preferentially detects bleeding in the lower bowel

and may miss bleeding higher up. In addition it may also detect blood from sources other than cancer, such as certain foods, piles, colitis and polyps. Such false positives influence the sensitivity of the test as a useful tool for screening because all positives whether true or false will go on to have more tests. Some will also suffer from unnecessary anxiety and investigation. In addition screening tests fail to detect some cancers and these are false negatives (specificity). Accordingly some people with cancer may not be detected and this affects the efficiency of the programme.

IS SCREENING WORTHWHILE?

Once a reliable test has been found, it is necessary to decide whether screening is worth doing. This requires consideration of the test method the people to be tested, the benefits and feasibility of screening.

The following is a list of some of the criteria which have been used to assess a screening programme which may be helpful to consider.

1. The disease should be of national importance. As the second most common cause of cancer death there is no doubt that this disease fulfils this criterion.

2. The natural history should be understood. As with most cancers the natural history is poorly understood. The first problem is that the screening test currently in use also detects polyps . It is not known whether screening will preferentially detect those polyps at high risk nor if the removal of cancerous polyps will improve survival. The second problem is that the natural history of this cancer is not understood . Many older people dying from other causes are found to have undetected cancers on postmortem examination which have never given rise to symptoms in their life-time. Screening may also detect slow growing cancers which have no life-time risk thus exposing the individual to unnecessary investigation and treatment.

3. There should be a recognisable early stage. The early stage of cancer is the polyp but, apart from surgical removal and examination under the microscope is it possible to identify those polyps which will become cancerous? Since the majority of polyps are innocent this raises a difficult ethical question about treating people unnecessarily.

4. There should be an effective test. The haemmocult test reacts to blood in the bowel. An ideal test should yield as many cancers as possible and have as few false positives and negatives as possible. It is still not known what proportion of cancers the test detects. From postmortem studies the prevalence of cancer has been calculated. In some age groups the prevalence of polyps

is as high as 50% and of cancer 1%. It would be necessary to compare these sort of data with the screening test to see what the yield of cancers and polyps is and to estimate its reliability.

5. There should be an effective treatment for the disease. There is no effective cure for the majority of patients as most present too late for this to be possible. The argument is therefore that treatment at an early stage should be of more benefit than treatment later on . Treatment of late cancer does not alter the 5 year survival of 30% but does treatment of earlier stages improve survival? Lead time bias is where early detection of cancer simply means that the individual lives with the knowledge of cancer for longer rather than experiencing improved survival. The current experimental trial testing whether earlier treatment improves survival compared to later treatment may resolve this controversy.

6. Facilities should be available for diagnosis and treatment. Because screening programmes generate work, increased resources are required for diagnosis and treatment. Does this mean that other types of service provision have to be given up?

7. Screening tests should be acceptable to the population. A true measure of acceptability is reflected partly in the compliance ie the number of people who come forward for the test. If a

screening programme is going to justify the resources it will have to have a high uptake. Some people may not wish go on the restricted diet necessary for the test nor have the anxiety of a test. In addition a test raises the possibility of further investigation and all that that implies. Often subjects do not realise what they may be in for at the start of investigations and this may generate its own problems.

8. There should be an agreed policy on whom to treat. Is there a consensus amongst clinicians as to what the best approach to polyps is or indeed is there a consensus on treatment of the different stages of the disease?

9. Case finding should be a continuous process. A major problem is that screening first yields a large number of existing cases rather than new cases. Will screening detect early new cases rather than simply existing late cases? Another problem is that rapidly growing cancers present in the intervals between screens whereas slow growing cancers will be detected early. This is known as length bias. Paradoxically therefore, the most malignant tumours may escape the screening programme whereas the least malignant(with their better prognosis anyway) will be found. Screening programmes must be set at intervals to maximise the potential for capturing new cancers.

Screening is not easy there are all sorts of complicated issues and questions which need to be asked. These include:

* Are patients clear that the present screening trials are about measuring the effects of early treatment?

* What is the yield of early cancers in the population screened compared with those in the population who present with symptoms?

* What is the yield of polyps?

* Does early treatment of polyps reduce the mortality from cancer?

* Does early treatment of cancer reduce the mortality of disease?

* What should the interval between screening tests be?

* What is the size of the target population?

* Is cancer screening feasible or will it result in the running down of other services?

* Is it economically worthwhile?

Economics

In our own lives we are faced with financial decisions. What we spend our money on is important in determining what we can and cannot have. Similarly in health care the resources are finite and thus decisions have to be made about programmes of health care. There are three aspects to the economics of screening. The first is that the project has to demonstrate that it is worth doing; secondly that it is more worthwhile than any other competing projects; lastly that it is feasible. This applies to any project whether it be screening, family cancer clinics or treatment programmes. Too often new innovations are introduced into the health service without prior consideration of the impact on other service provision.

i. Is the Project Worth Doing?

If we look first at the programme itself, clearly a programme is only worth doing if the benefits outweigh the costs . The costs have to take into account diagnosis, treatment and resources, the costs to the patients in terms of time off work, anxiety, access and travel. Costs also include the fact that all procedures carry their own risks of illness. For instance colonoscopy, the internal inspection of the bowel, carries with it a small risk of perforation and the radiological examination of the bowel by barium enema carries its own tiny risks of cancer. The benefits are in what the programme is trying to achieve. In the case of prevention it is improved

survival. This is clearly a dilemma because it seems impossible to put a value on life. The reality is that this is always done either explicitly or implicitly. For example in building the channel tunnel a predicted number of people will die and this has been accepted within the economic evaluation of the project.

ii) How does the programme compare with other projects.?

Even when a programme is considered to be beneficial the next stage is to compare it against the benefits of other programmes. This is called the "opportunity cost" where the adopted project could mean the loss of a programme elsewhere. Thus, the introduction of a screening programme or a family cancer clinic programme could mean a reduction in the funding for an alternative project eg care of the elderly or heart transplants. It is for this reason that it is essential to measure what is done and know why we are doing it.

Comparing programmes is difficult; how can the value of hip replacements be compared with the value of a treatment programme or a screening programme? It is clearly difficult to do and standard measures are required to find a universal or translatable measure.

iii) Is the programme feasible?

Even if a programme is considered to be worthwhile it has to be determined whether it is feasible.Not only is there competition with other programmes of care but there may be competition for current resources. For example a screening service for cancer means an increased workload for nurses, clinicians and pathologists and also competition for physical space. Clearly if there is no give in the system this will mean that something else may be neglected. If gastroenterologists, say, are deployed onto the service then they will obviously not be available to do other types of work eg.for ulcer patients or other referrals for investigation. This is currently the situation in the breast screening programme where a failure to recognise the implications of service provision has detracted from current services for women.

The questions that the audience will be thinking about ought to include.

* Have all the costs of the programme been counted?

* Do the benefits of the programme outweigh the costs?

* How do the benefits of the programme compare with the benefits of other programmes?

* What are the resource implications of the programme?

* How will other services and patients be affected by additional service provision.?

Tertiary Prevention

The aim of tertiary prevention is to prevent the complications of the disease when it has presented . This could be to prevent obstruction of the bowel due to local spread or jaundice and liver failure due to distant spread or to prevent the symptoms of pain. This is considered under the section on treatment.

SECTION 4.

Treatment

The Aims

There are only two aims of treatment of cancer of the colon and rectum: these are the intention to cure which includes the relief of symptoms, and palliation which is the relief of symptoms alone. Reviewed cancer registration data indicate that 40% of patients die without receiving treatment . In some patients this may be because of late presentation:for instance some 15% of people have the same date of registration and the same date of death. However, it is not yet possible to identify from the national cancer registration data which of the patients in the untreated group have had symptom relief. These are some of the questions that need to be answered. *Are clinicians and patients aware at all times of the aims of treatment? *How can patients and clinicians find out about the effectiveness of symptom relief?

Types of treatment

1. Surgery

Of all the patients diagnosed as having either cancer of the colon or the rectum 60% will go on to have surgery, some for relief of symptoms such as obstruction and others with the aim of cure. In those patients who undergo surgery with the aim of cure some may have the option of additional supportive therapy known as adjuvant therapy. Patients undergoing surgery have part of their bowel removed. If the cancer is very low down or widespread then the patient may have an operation which results in a colostomy. A colostomy is the result of a hole being made in the abdominal wall and the bowel contents exit through a bag rather than out through the rectum. Fewer people today have colostomies because new techniques have resulted in a dramatic increase in sphincter saving operations. In addition there are newer techniques such as colonic pouches which should reduce the risk of faecal incontinence in those patients undergoing surgery.

* Are patients adequately informed about the different therapeutic options available and the risks and benefits of different treatments?

2. Adjuvant therapy

The role of adjuvant therapy is to prolong remission or sustain cure as an adjunct to the main treatment surgery. The aim of therapy is twofold: to prevent the recurrence of disease locally and to prevent metastasis. Metastasis is the remote spread of tumour to other parts of the body. Three types of adjuvant therapy are commonly used: radiotherapy, chemotherapy and immunotherapy. Radiotherapy is given locally at the site of the tumour, chemotherapy and immunotherapy are given systemically into the blood stream. Radiotherapy is normally only used in rectal cancer but chemotherapy and immunotherapy may be given in both colon and rectal cancer. The value of all these adjuvant therapies is still being tested in large randomised clinical trials. When assessing the benefits and indications of any therapy whether surgical or adjuvant, rectal and colonic cancer must be considered separately.

However there are questions that still need to be answered:

* Have the benefits of adjuvant therapy been established?

* What are the indications for adjuvant therapy and when should it be given?

Quality of care

Quality of care starts at the time of presentation and continues through diagnosis to treatment, cure and follow up or to death. This is the care that a patient can expect to receive whether the treatment is intended to cure or is palliative.

* Are all clincians sufficiently well informed of the progress in treatment?

* Is there a place for standardised, universal treatment protocols?

i. Surgery

While current treatment schedules are unlikely to have a dramatic impact on survival it is becoming clear that there may be other aspects of treatment which determine survival. Variations in survival have been observed internationally with Britain having some of the lower survival rates observed in Western Europe. Even within Britain variations exist in overall survival between regions which cannot be accounted for just by differences in disease presentation. Emergency admissions have a worse survival than elective or arranged admissions all of which cannot be accounted for by late presentation. In America it is estimated that if all patients received "state of the art" treatment then mortality could be reduced by 20% for cancer of the colon and 39% for cancer of the rectum by the year 2000. This would have the effect of saving many thousands of lives.

Some of the questions that need to be answered include?

* What are the reasons for the international differences in survival from colorectal cancer.

* What is the contribution of the clinician to the observed national variations in survival?

* What is the potential for "state of the art" criteria to improve survival in Britain ?

* In addition to improving current standards of treatment are there other issues around the quality of care which need to be considered such as the patient experience of hospital admission, subsequent investigation and follow up and the information received?

Adjuvant therapy

Service delivery is an important component of care. Most adjuvant therapy is carried out in specialist centres where patients attend as day patients or out patients. Adjuvant therapy can and does place an

enormous burden encroaching upon patients lives raising the following questions:

* Is current service provision being tailored to the patients needs?

* What are the components of good service provision?

Colostomy

Many people still associate cancer of the colon and rectum with colostomy. Nowadays fewer people require colostomy due to improved and new surgical techniques however there are still a large number of people who are living with a colostomy. In addition cancer of the large bowel has traditionally been a stigmatising disease and patients have to come to terms with cancer itself as well as the disability experienced by some with a stoma.

Palliative care

For many years providers of terminal care support have been at the forefront of ensuring quality of care and quality of life. Many hospices now report that cancer of the colon and rectum is the leading cause of admission. Current survival rates mean that less than 30% of people diagnosed with cancer of the colon and rectum survive 5 years and so palliative care is of increasing importance.

* What is the role of palliative and nursing care and how can other service providers learn about the approach of the terminal care team and the resources they have at their disposal?

Quality of life

Quality of Life is the goal of all treatment . Unlike survival, quality of life is not a measure of time. It is the ability of the individual to enjoy a rich and fulfilled life with in the constraints of the disease. Many of the quality of care issues discussed influence directly the quality of the patients life.

In order to assess the quality of life properly every patient should be assessed individually .There are problems about standardising subjective data to ensure that the findings relate not just to the individual but to the disease process. Data must be valid , repeatable and reliable. Some examples of the aspects that are being researched include the resumption of sexual activity, work and recreation after treatment.This is in addition to the other measures of the side effects of treatment. Surgery is now becoming less invasive and new techniques have meant that more patients are having sphincter saving operations This has resulted in a dramatic fall in the colostomy rate in many parts of the country. Nevertheless large bowel surgery does result in considerable morbidity for instance impotence and patients still have to come to terms with increased morbidity and social disruption even in the absence of a stoma.

Because the benefits of adjuvant therapy are not yet proven large randomized clinical trials may continue to be of importance.

This raises several issues which include:

* What is the role of randomised clinical trials?

* Is there sufficient patient information and consultation about treatments and trials?

* Is there sufficient consideration of the effects of treatment on the quality of life?

* What economic appraisal has been performed of treatment options?

* What are the resource implications of current trials and treatments?

* Do current trials sufficiently consider the patient and their family the quality of care and the quality of the patients life?

CONCLUSION

Remarkable progress in new surgical techniques can minimise the impact that cancer of the colon and rectum has on peoples lives . Similarly advances in the field of radiotherapy and chemotherapy provide hope that survival may be prolonged. If the progress that is being made is sustained and the standards of care and delivery of service are achieved then patients can expect not only improved survival but good quality of life which is the goal of all treatment. These are some of the issues that members of the audience may wish to think about throughout the conference.

JRP