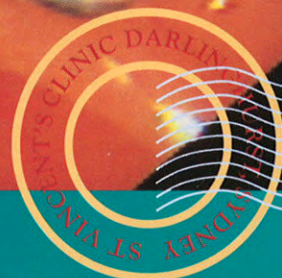
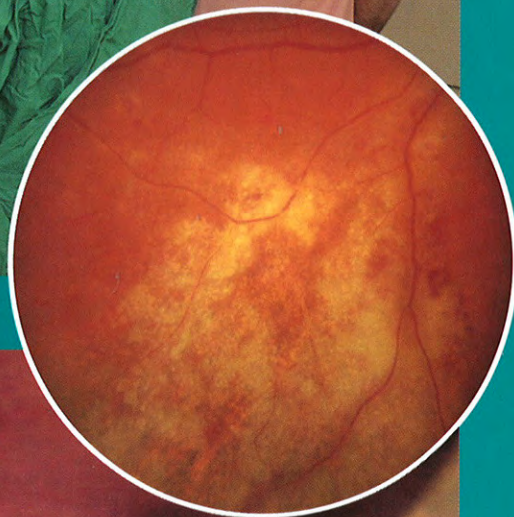


PROCEEDINGS



ST VINCENT'S CLINIC, SYDNEY

VOLUME 3 No:1 JULY 1995



INSIDE THIS ISSUE...

OPHTHALMIC MEDICINE &
SURGERY

COLON & RECTAL SURGERY

BREAST CANCER

ENDOSCOPIC BILIARY
REVOLUTION

ORTHOPAEDIC SURGERY



PROCEEDINGS

Editorial <i>Dr John Roarty</i> <i>Medical Executive Officer</i>	2
Scientific Council's Recommendation for 1995 Research Grants	3
Reflections on Colon and Rectal Surgery: A 1995 Perspective <i>Dr Terence O'Connor</i>	4
Recent Advances in Ophthalmic Medicine and Surgery <i>Dr Michael Delaney, Dr Ross Fitzsimons,</i> <i>Dr Peter McCluskey, Dr Justin Playfair</i>	9
Minimally Invasive Orthopaedic Surgery <i>Dr Brett G Courtenay</i>	15
Breast Cancer Strategies for Care – Operable Disease <i>Dr Michael Jensen</i>	19
The Endoscopic Biliary Revolution <i>Dr David Byrnes, Dr Anthony Davies,</i> <i>Dr Paul Edwards, Dr Stephen Mistilis,</i> <i>Dr Chris Vickers</i>	24

COPYRIGHT

All literary matter in the Journal is covered by copyright, and must not be reproduced, stored in a retrieval system, or transmitted in any form by electronic or mechanical means, photocopying, or recording, without written permission.



ST VINCENT'S CLINIC



BOARD OF DIRECTORS

Mr Peter Ferris (Chairman)
Sr Clare Nolan, RSC (Secretary)
Mr Jim Baillie
Dr Russell Aldred
Dr Brett Courtenay
Professor James Biggs
Dr Michael Burns
Mr Ted Harris, AC
Sr Rose Holman, RSC
Mr William Hyde
Dr Donald Maxwell
Dr David Wilson
Dr John Roarty
(Medical Executive Officer)

CONGREGATIONAL REPRESENTATIVE

Sr Mary Bernice Elphick, RSC, AM
OBE

MEMBERS OF THE MEDICAL COUNCIL

Dr Donald Maxwell (Chairman)
Dr Brett Courtenay (Secretary)
Dr Russell Aldred
Dr Michael Burns
Dr Paul Kelly
Dr David Wilson

ST VINCENT'S CLINIC FOUNDATION

MEMBERS OF THE BOARD OF TRUSTEES

Sr Mary Bernice Elphick, RSC, AM,
OBE, (President and Chairperson)
Mr Peter Falk
Mr Peter Ferris
Mr Arthur Fitzgerald, AM
Mr Ted Harris, AC
Professor John Hickie, AO
Dr Thomas Hugh
Mrs Leith Myerson, MBE
Dr Donald Maxwell
Mrs Roslyn Packer
Dr Diana Shogren
Professor Douglas Tracy, AO
Mr Peter Whalan
Mrs Inn Wei Mok (Secretary)

PATRON

Sir Roden Cutler, VC, AK, KCMG,
KCVO, CBE

MEMBERS OF THE CLINIC FOUNDATION MEDICAL SCIENTIFIC COUNCIL

Dr Donald Maxwell (Chairperson)
Professor John Hickie, AO
Dr Thomas Hugh
Professor Douglas Tracy, AO

ADDRESS

ST VINCENT'S CLINIC
438 Victoria Street, Darlinghurst, Sydney, NSW 2010, Australia
Phone: (02) 332 6222 Fax: (02) 332 7234

EDITORIAL

Dr John Roarty

MEDICAL EXECUTIVE OFFICER



Colo-rectal cancer is one of the main causes of death in the Australian population today. Breast cancer is the most common malignancy in women in the country with approximately one in thirteen likely to develop this cancer by age 75.

The influence of genetic mutation in the aetiology of malignant disease in the lower gastro-intestinal tract has opened up a new field in the study of the causation and early detection of this disease. It may determine when a colitic colon requires prophylactic resection. Molecular genetic analysis could determine which patients are at risk of recurrence and thus require adjuvant therapy. The clinic's Department of Colon & Rectal Surgery is conducting research to develop a screening assay to detect the presence of mutant genes in nearly half of colo-rectal cancers at a stage when they are curable by surgery alone.

Molecular genetics is also showing signs of understanding the cause, spread and treatment of breast cancer. When available, gene testing should assist in its management especially in the pre-menopausal group. At the Clinic, Dr. Jensen outlines the best therapy for breast cancer provided within a multi-disciplinary team, including surgical, radiation and medical oncologists. Of interest, the commonest hereditary syndrome is an association of breast cancer with colonic cancer (described above) both occurring in a younger than expected age group.

The revolution in endoscopy procedures for diseases of the upper gastro-intestinal tract is a great benefit to mankind. Dr. David Byrnes and his partners in the Diagnostic Endoscopy Centre give hope and comfort to these people suffering from pathology in the stomach, duodenum, pancreas and gall bladder. These procedures are usually

carried out on a day basis and a visit to the Endoscopy Centre.

The increasing trend for the need for day surgery services is also emphasised by Dr. Courtenay. Relief from distress from so many joint disorders - osteoarthritis, cartilage tears and ligament damage, can now be performed as an outpatient.

The rapid advances in the field of ophthalmology are outlined by Dr M. Delaney and his colleagues. The new concept of insertion of an intra-ocular lens to cure cataract disease is now accepted and safe. The close relationship the ophthalmic surgeons have with other specialists in neurology and otology in the new discipline of skull base surgery is another indication of the need for a multi-disciplinary approach to difficult problems which all patients can enjoy in attending St. Vincent's Clinic.

St Vincent's Clinic Foundation

Scientific Council's Recommendation for 1995 Research Grants

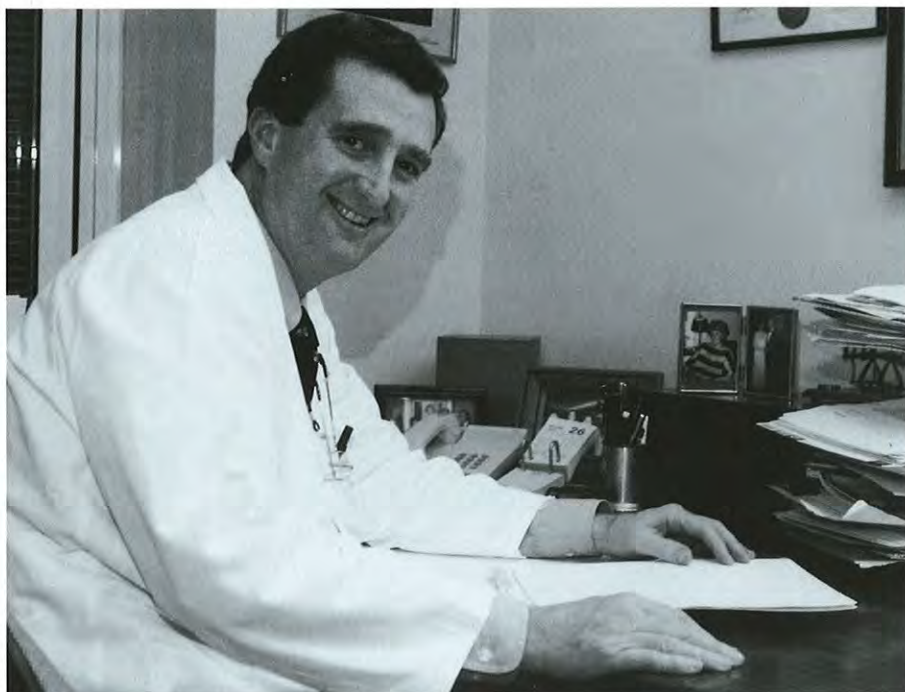
Project Title

Chief Investigator

- | | |
|--|--|
| 1. To investigate the role of oncogenes and tumour suppressor genes in normal prostate, benign swelling of the prostate and prostate Cancer. | Dr John Grygiell
SVC Urology Department |
| 2. The Development of Chronic Xenograft Rejection. | Dr Phillip Spratt |
| 3. Bone densitometry in prediction of loosening of artificial hips (3rd year) | Dr Nicholas Pocock |
| 4. The effect of hormone replacement therapy on blood vessels, stiffness, aspects of blood fat metabolism, abdominal obesity and aspects of blood sugar central in women after menopause who have maturity onset diabetes. | Dr Ray Kelly |
| 5. Importance of Salt Transport to the Normal Functions of Cells Lining the Walls of Blood Vessels. | Professor Terry Campbell |
| 6. The normal function of genes involved in the initiation of colon cancer. | Dr James Williamson |
| 7. Progressive tissue damage by blocking the arterial supply with microscope beads. | Professor Reginald Lord |
| 8. Genetic Engineering of Antibodies against Bowel Cancer. | Dr Alan Meagher |
| 9. Studies of tumour cells death in Bowel Cancer. | Dr Terence O'Connor |

Dr Terence O'Connor

Reflections on Colon and Rectal Surgery: A 1995 Perspective



The origin of colon and rectal surgery is attributed to Frederick Salmon, who in 1835 founded his own institution "The Infirmary for the Relief of the Poorly Afflicted with Fistula and Other Diseases of the Rectum", which was the forerunner of St. Mark's Hospital, London, England. In the United States, Joseph Matthews studied at St. Mark's Hospital in 1878 and on returning to Louisville, Kentucky, he became America's first fulltime proctologist. In 1899, Matthews was unanimously elected as the first president of the American Proctologic Society, now named the American Society of Colon and Rectal Surgeons.

The Section of Proctology was formed within the Australian College of Surgeons in 1963 and it became known as the Section of Colon and Rectal Surgery in 1968. The first Australian Fellow in Colon and Rectal Surgery was enrolled in 1989. The first Colon and Rectal Unit in Australia was established at Sydney Hospital in 1971 with Dr. Edward Wilson, Dr. David Failes and Dr. Mark Killingback. In 1976 Dr. Mark Killingback became the first surgeon in Australia to declare himself publicly as solely practising in colon and rectal surgery. The Sydney Colorectal Surgical Society was formed in 1983 and the Australian Colon and Rectal Surgical Society in 1988. Dr. Les Bokey became the first and only full professor in colon and rectal surgery in Australia in 1991.

Dr Terence O'Connor FRCS, FRACS

Colo-rectal Surgeon
St Vincent's Clinic

MOLECULAR GENETICS

In 1995 there are several aspects of colon and rectal surgery which are exciting interest worldwide. The first of these, and possibly the most important, is molecular genetics. There has been an increased recognition that colorectal cancer is frequently a familial disease. While the Mendelian dominant inheritance of familial adenomatous polyposis (F.A.P.) has long been recognised, this disorder accounts for only 1% of all colorectal cancers. More recently, Lynch has identified the syndrome of hereditary nonpolyposis colon cancer (H.N.P.C.C.) which is also transmitted by dominant inheritance. This disorder, characterised by colorectal cancer in three or more relatives in two or more generations, accounts for roughly 4 - 13% of all colorectal cancers. Typical features of H.N.P.C.C. patients include young age of onset, frequently less than 50 years, frequent synchronous and metachronous tumours, a right sided predominance of tumours and a relatively good prognosis. Associated cancers in some, (Lynch II) H.N.P.C.C. kindreds include endometrial, gastric, biliary, pancreatic and genitourinary.

These colorectal cancers are monoclonal rather than polyclonal in nature. That is to say, the neoplastic epithelium of a given colorectal tumour, benign or malignant, arises from a single progenitor cell. Thus a single mutation confers a growth advantage to one cell that leads to hyperproliferation and development of a visible polyp. A second mutation may then confer an additional growth advantage and this clone of cells will overgrow the first. One can see how this sequence of events culminates in the clinical evolution of normal mucosa to hyperproliferative mucosa to benign adenomas to carcinomas.

Genes responsible for malignant transformation have classically been divided into two groups; oncogenes and tumour suppressor genes. More recently a third type of mutated gene that promotes genetic instability in numerous loci has been identified. Homologous genes with normal physiologic functions (proto-oncogenes) in an activated form become cellular oncogenes which cause human tumours. Oncogenes act in a dominant fashion because alteration of only one allele is necessary to cause cellular effect. Examples of oncogenes include K-ras, myc and src.

In contrast to oncogenes, tumour suppressor genes inhibit cellular proliferation and tumourigenesis. Loss of these genes typically has recessive action in that both alleles must be lost in order to see an effect. The P53 repressor gene is an exception to this rule in that its mutated protein product binds and this inactivates the wild type gene product. Other examples of tumour suppressor genes important in colon and rectal cancer include the A.P.C. gene (adenomatous polyposis coli), M.C.C. gene (mutated in colon cancer) and D.C.C. gene (deleted in colon cancer).

Genes localised to the short arms of chromosomes 2 and 3 cause widespread instability at numerous loci. Typical changes include variations in length of microsatellite D.N.A., short repetitive D.N.A. sequences located throughout the gene arm. The mutated genes responsible for these abnormalities normally function to recognise and repair D.N.A. replication errors. Mutations of these two loci appear to be responsible for roughly 80% of all H.N.P.C.C. cancers.

In addition, microsatellite instability has been identified in 13% of sporadic colorectal cancers.

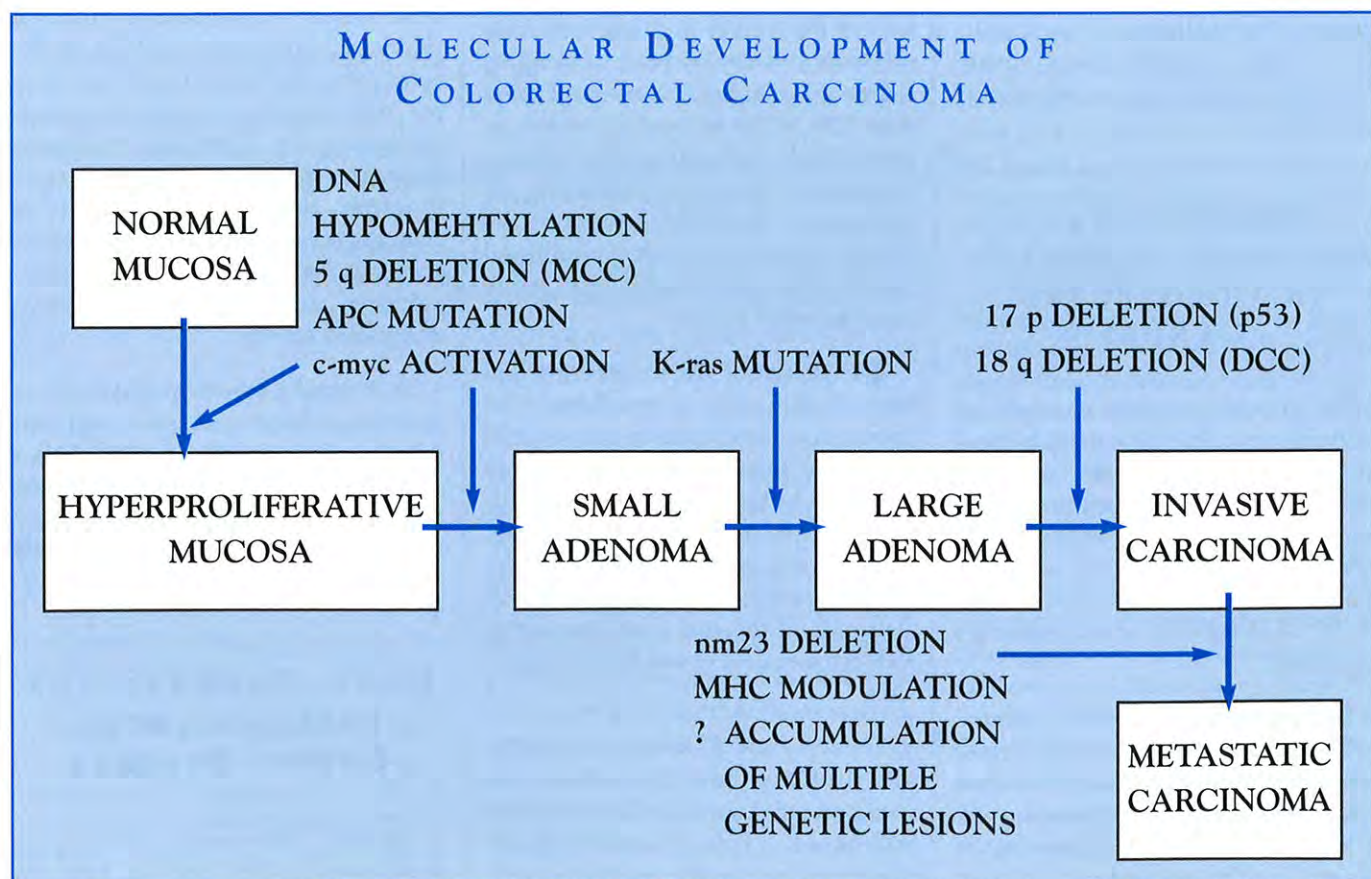


Figure 1

The current understanding of colorectal carcinogenesis is largely the work of the John Hopkins Large Bowel Cancer Group headed by Bert Vogelstein. Vogelstein's model is depicted in Figure 1. Central to this model is the notion that cancer is caused by an accumulation of mutations including both oncogene activation and tumour suppressor gene inactivation. In the case of familial adenomatous polyposis, a germline mutation of the A.P.C. gene allows a single mutation of its other allele to cause hyperproliferation and polyp formation.

Clinical application of this new knowledge, whilst not yet routine, is imminent. Peripheral blood leucocytes can be analysed for the A.P.C. gene to identify presymptomatic F.A.P. patients. Screening of the faeces of patients with colorectal neoplasms for R.A.S. gene mutations may prove more specific than faecal occult blood testing.

Genetic analysis may supplant histologic assessment for dysplasia to determine when a colitic colon requires prophylactic resection. Molecular analysis may eventually determine which patients are at risk for recurrence and thus require adjuvant therapy.

Finally, identification of specific genetic abnormalities will eventually allow gene transfer and other pharmacological and immunologic approaches.

MONOCLONAL ANTIBODY SCANNING IN COLORECTAL CANCER

The concept of using monoclonal antibodies in colorectal cancer is based on the principle that an antibody directed against an antigen present on colon cancer cells is tagged with radioisotope and injected intravenously. Murine monoclonal antibodies bound to IN111, I125 or 99mTc are currently being used.

Such approaches have shown that the test is sensitive for detecting pelvic recurrence, indeed more sensitive than C.A.T. scanning. It is, however, not as accurate as C.A.T. scanning in detecting intrahepatic disease.

Currently, such techniques are experimental and require increase in sensitivity and accuracy before they come into more general use.

ANORECTAL A.I.D.S. AND H.P.V. INFECTION

Human papilloma virus (H.P.V.) is now the commonest venereal disease seen in surgical practice. This venereally transmitted virus creates a field defect which can involve the entire perineum, anal canal and at times the rectum. In the female, it can involve the vagina and cervix and in both male and female, the distal urethra. Accurate, successful treatment requires eradication of the virus in all sites. Laser obliteration with local anaesthetic blocks and 5-fluorouracil creams in more sensitive sites can be effective in treatment but there is a 20 - 30% recurrence rate. There is now a clear association between H.P.V. infection and squamous cell dysplasia and carcinoma in situ (Bowen's disease). The end point in this progression is invasive squamous cell carcinoma. In treating Bowen's disease, careful mapping of the field with multiple biopsies in each quadrant at the level of the dentate line, anal verge and perineum is necessary prior to planning excisional treatment. Only if more than 50% of the perianal skin needs to be excised, will skin grafts become necessary. Invasive squamous cell carcinoma is preferably treated by the Nigro regime, with combined radiotherapy and chemotherapy, rather than excisional surgery.

The advent of H.I.V. infection and the increasing numbers of immunosuppressed patients as a result of transplant surgery, has led to further increases in the incidence of H.P.V. infection and anal and perianal intraepithelial and invasive cancers. H.I.V. infection itself can be associated with ulceration of the anal canal, frequently with cytomegalovirus and herpes simplex virus.

There are now 57 subtypes of H.P.V. identified, 6 and 11 being the commonest found in condyloma acuminata. Types 16 and 18 are the ones most frequently associated with aggressive behaviour in neoplasia, hence

it is appropriate that hybridisation studies be performed to identify the patient at risk. This is particularly important in the patient who is H.I.V. positive but asymptomatic, with a prolonged survival expected.

ANAL ULTRASOUND FOR BENIGN DISEASE

The ultrasonographic appearances of the rectal wall consists of concentric alternating hyper- and hypo-echoic rings which correspond in part to the different anatomic layers. Within the anal canal, the anatomy of the anal sphincter muscular complex can be delineated.

Endoanal ultrasonography is emerging as the procedure of choice for anal sphincter mapping and imaging. It can be done as an outpatient procedure, is relatively quick and virtually painless. The internal anal sphincter appears endosonographically as a hypo-echoic circular band, seen most prominently at the level of the mid-anal canal. The external anal sphincter appears as a thicker, circular mixed echogenic band, outside of the hypo-echoic internal sphincter. Other structures of the pelvic floor, such as the puborectalis, urethral sphincter, vagina and outlines of the bony pelvic and ischio-rectal fossae can be demonstrated with endoanal ultrasonography. There is no correlation between sphincter thickness and function but it is excellent in demonstrating sphincter defects which correspond with decreased manometric pressure and decreased electromyographic activity.

Endorectal ultrasonography is being used to help stage rectal cancer and large villous tumours of the rectum. It is a relatively effective way of determining depth of wall invasion but is only 75% accurate in determining lymph node status.

DRUG THERAPY FOR INFLAMMATORY BOWEL DISEASE

Perhaps the most interesting development in this field has been the use of Cyclosporin, which has been

shown to prevent colectomy in 53% of patients with ulcerative colitis who have shown a good clinical response in 1 month and 33% of patients at 12 months.

The good responders tend to be those with a long duration of disease and a normal haemoglobin level. It may be that the most important role for Cyclosporin will be to induce a remission in severe steroid resistant ulcerative colitis, allowing for a one or two stage total proctocolectomy and ileoanal pouch procedure rather than a three stage procedure.

Cyclosporin has also been used in steroid refractory Crohn's disease to induce remission but adequate trials and results are not yet available.

A gene abnormality has recently been demonstrated in Crohn's disease which has shown an abnormality of tumour necrosis factor. A monoclonal antibody to tumour necrosis factor has been developed which binds T.N.F., producing a remission in acute Crohn's disease. This is an experimental area which will be followed with interest.

SCREENING FOR COLON AND RECTAL CANCER

One in 25 people in Australia will develop colon and rectal cancer throughout their lifetime and this increases to 1 in 8 when there is a first degree relative in the family with colon and rectal cancer. Some form of national screening programme will be introduced in the future, focusing particularly on patients over the age of 50.

The Minnesota trial commenced in 1975, involved over 46,000 participants with a 13 year followup. There was a 33% reduction in colorectal cancer mortality in the group who had annual Haemoccult faecal occult blood screening compared to a control group. It may be that this test will be supplanted by faecal screening for colorectal oncogenes.

Flexible fibroptic sigmoidoscopy to 60 cms. will detect 60% of colon and rectal cancers and combined with a Haemoccult test, or in the future, faecal oncogene screening test, may prove to be a very accurate way of detecting colorectal cancer at an early stage.

ADJUVANT CHEMOTHERAPY

Mortell's study from the Mayo Clinic, published in the New England Journal of Medicine in 1990, established that 5-fluorouracil and levamisole for patients with Duke's C colon cancer, given over a period of 12 months, led to a reduction in risk of recurrent disease of 41% and reduction in the rate of death by 33%. This is now standard practice for Duke's C colon cancer patients and it is currently the Clinic's practice to give radiotherapy postoperatively, combined with chemotherapy for Duke's B and C rectal cancers.

THE ELECTRICALLY STIMULATED SKELETAL MUSCLE NEOSPINCTER FOR FAECAL INCONTINENCE

In 1952 Pickrell devised an anal wrap procedure that utilised transposed gracilis muscle based on an intact proximal neurovascular pedicle. Functional results with this operation proved poor, however, as patients were unable to maintain continuous voluntary contraction of the muscle. The gracilis muscle comprises predominantly Type II (fast twitch rapidly fatiguing) muscle fibres. The observation that fast twitch muscles can be converted to slow twitch fatigue-resistant fibre types by continuous electrical stimulation and the development of implantable electrical pulse generators, capable of providing such stimulation, has permitted development of the electrically stimulated skeletal muscle neosphincter (E.S.M.N.S.). This dynamic graciloplasty is maintained in a tonically contracted state until patients wish to defaecate, at which time the pulse generator is deactivated by a hand held magnet and the muscle relaxes. Currently the technique is reserved for severe endstage incontinence patients where all other techniques have failed.

LAPAROSCOPIC COLECTOMY

Apart from molecular genetics, no other facet of the specialty has consumed so much interest over the last 4 years. The initial articles concerning laparoscopic colectomy were published in early 1991 and generated a lot of early enthusiasm. It is a much more difficult procedure, however, than laparoscopic cholecystectomy as it involves working in multiple abdominal quadrants, full mobilisation of the colon, division of the mesentery and usually an anastomosis. An incision is required to remove the specimen and an anastomosis is involved with its attendant morbidity.

Reports of early abdominal wall port site recurrence following laparoscopic surgery for cancer are very disturbing. It is standard practice to operate for colon and rectal cancer with a wound protector to prevent malignant contamination of the wound and since the advent of this precaution, wound recurrence in colon and rectal cancer surgery is anecdotal.

With laparoscopic surgery, ports are placed unprotected into the abdominal cavity and simple irrigation with Betadine on withdrawal of the port may well not be adequate to prevent malignant contamination. The operation is carried out in a vapour of water from irrigation, mixed with blood and lymph and is an ideal situation to implant malignant cells into abdominal wound sites.

It is clear that port site recurrences have occurred, both at the site of specimen removal as well as ports remote from the removal site. A great deal more investigation is needed into this important area.

Randomised controlled trials are necessary to make a cost benefit analysis.

Certainly laparoscopy has a very definite role in staging the extent of cancer and in the formation, for example, of a defunctioning ileostomy. I suspect it will have a significant role in the management of rectal prolapse, performing a posterior rectopexy (Ripstein procedure) and in simple cases of obstruction due to single or two or three band adhesions only. Certainly instrumentation is being improved

almost monthly and the development of three dimensional imaging and virtual reality may have a further significant impact.

DAY ONLY SURGERY

Fully 40% of surgical procedures can now be done on a Day Only basis and the Unit is currently performing Day Only haemorrhoidectomy, utilising a mixed plication-excisional technique with Marcin blocks and nonsteroidal anti-inflammatories. In addition, pilonidal sinus, anal fissures, simple fistulas, perianal abscesses and skin tags are all being managed on a Day Only basis. I believe the new dipolar laser will make such surgery even more feasible.

ST. VINCENT'S CLINIC DEPARTMENT OF COLON AND RECTAL SURGERY RESEARCH ACTIVITIES

Currently the Unit is actively involved in research projects with Dr. Robyn Ward in the Department of Oncology/Haematology.

1. One project seeks to develop a rapid and simple screening assay based on our understanding of the gene abnormalities in colorectal cancer.

Ideally this test will accurately detect the presence of mutant genes in nearly half of all colorectal cancers at a stage when they are curable by surgery alone.

2. A second project uses recombinant antibody techniques, human immunoglobulin gene libraries and phage display methodology to produce recombinant human antibody fragments with binding specificity for antigens displayed on the surface of colorectal carcinoma cells. These antibodies which bind the colorectal tumour cells will be characterised with reference to their potential as diagnostic or therapeutic agents in colorectal cancers.

3. Over the past decade a variety of biological features of colorectal cancer have been assessed for their value in predicting disease outcome. D.N.A. ploidy status of adenomas has been shown to be an unreliable predictor of malignant change and whilst studies on

colorectal cancer have shown that individuals with diploid tumours have a better prognosis, it in itself is not an independent prognostic factor. The term, "apoptosis", coined by Kerr in 1972 refers to the process of programmed or physiological cell death. Unlike necrosis, cell death due to apoptosis occurs in an orderly manner and is not associated with an inflammatory response. It is a morphologically distinct process in which the cell undergoes rapid nuclear and cytoplasmic shrinkage followed by formation of discrete fragments which are ingested by surrounding cells. The process can be recognised unequivocally at an ultrastructural level and with less viability by light microscopy.

This D.N.A. fragmentation has been used as the basis for the Tunel Assay, which allows the sensitive and specific detection of apoptotic cell death in histological sections. Normal cells respond to D.N.A. damage by either delaying their division until the damage is repaired or by undergoing apoptosis. This mechanism thus ensures the elimination of genetic variance with potentially enhanced neoplastic potential.

The failure of apoptosis has been shown to promote the development of neoplasia by allowing cells with mutated D.N.A. to progress through the cell cycle. A number of oncogenes have recently been shown to mediate their effect through the inhibition of apoptosis, although little is known of the molecular events which signal this event.

The P53 gene, mutated in 70% of human colorectal cancers, is a very important regulator of apoptosis. Normal or wild type P53 halts the cell cycle in G1 phase, thereby allowing time for D.N.A. repair prior to cell division. If the D.N.A. damage is irreparable, the cell becomes committed to the apoptotic pathway. Mutation of the P53 gene allows escape from this surveillance mechanism and the generation of the malignant phenotypes. Recent studies have shown that the frequency of P53 mutations in colorectal cancer correlates with prognosis.

Our current study, being carried out by Dr. Robyn Ward in the Department of Oncology, aims to determine the prevalence of apoptotic cell death in the various histological grades of colorectal

neoplasm and correlate this with clinical outcome. In addition the study will determine the presence of mutations of P53 and correlate this within the extent of apoptotic cell death.

ANAL PHYSIOLOGY LABORATORY

Dr. Alan Meagher has established, with the help of a Grant from the St. Vincent's Clinic Foundation, an Anal Physiology Laboratory which is invaluable in the assessment of patients with faecal incontinence, traumatic sphincter injuries, rectal prolapse and associated incontinence, and in helping to categorise patients with intractable constipation.

In conclusion, colon and rectal surgery is a rapidly expanding speciality with further crucial advances in molecular genetics and laparoscopic surgery ensuring an exciting future.

REFERENCES :

1. Vogelstein B Fearon ER Kearns SE et al: Allelotype of Colorectal Carcinomas. *Science* 1989;244:207-211
2. Vogelstein B Fearon ER Hamilton SR: Genetic Alterations During Colorectal Tumour Development. *N Engl J Med* 1988;319:525-532
3. Pickrell KL Broadbent TR Masters FW Metzger JT: Construction of a Rectal Sphincter and Restoration of Anal Continence by Transplanting Gracilis Muscle: Report of 4 Cases in Children. *Ann Surg* 1952;135:853-862
4. Salmons S Henriksson J: The Adaptive Response of Skeletal Muscle to Increase Use. *Muscle Nerve* 1981;4:94-105
5. Guillou PJ Darzi A Monson JRT: Experience with Laparoscopic Colorectal Surgery for Malignant Disease. *Surg Oncol* 1993;2(suppl):43-49
6. Fusco MA Paluzzi MW: Abdominal Wall Recurrence After Laparoscopic Colectomy for Adenocarcinoma of the Colon: Report of a Case. *Dis Colon Rect* 1993;36(9):858-861
7. Alexander RJT Jaques BC Mitchel KG: Laparoscopically Assisted Colectomy and Wound Recurrence. *Lancet* 1993;341:249-250
8. Mandel JS Bond JH Church TR et al: Reducing Mortality from Colorectal Cancer by Screening for Faecal Occult Blood. *N Engl J Med* 1993;328:1365-1371
9. Mortel CG Fleming T MacDonald J et al: Levamisole and Fluorouracil for Adjuvant Therapy of Resected Colon Carcinoma. *N Engl J Med* 1990;322:352-358
10. Kerr JFR Wyllie AH Currie AR: *Br J Cancer* 1972;26:239-257
11. Gavrieli I Sherman Y Ben-Sasson SA: *J Cell Biol* 1992;119:493-501

Dr Michael Delaney

Dr Ross Fitzsimons

Dr Peter McCluskey

Dr T Justin Playfair

Recent Advances in Ophthalmic Medicine and Surgery

Ophthalmic surgery has been one of the fields to benefit most from modern technological advances.

These advances have allowed the development of micro surgical techniques which now used in so many fields were often first used in ophthalmic surgery. There has been a steady reduction in the size of the wounds required to carry out all forms of ophthalmic surgery, but in particular cataract surgery. Modern ultrasound techniques allow the intraocular lens power assessment to become very accurate giving the patient the luxury of having an input into their post operative refractive state. Lasers are used extensively in ophthalmology, especially in the treatment of retinal diseases of which diabetic retinopathy and age related macular degeneration are the most common. The use of lasers in refractive surgery has allowed this subspecialty to become an accepted field in ophthalmology.

The Eye Department of St Vincent's Hospital and St Vincent's Clinic has helped introduce many of the changes in ophthalmic surgery and ophthalmic medicine. The Department has the leading clinic in ocular immunology in the country and is recognised for its teaching of medical and neuro ophthalmology. The Department has had the advantage of a close association with other departments on the campus. This association is obvious in medical ophthalmology and the Department has worked closely with the Otology and Neurosurgery Departments in the treatment of patients following complicated base of skull surgery, as well

as working harmoniously with the Plastic Surgery Department in the treatment of complicated cases.

The effect of modern technology has been to allow the introduction of a number of areas of subspecialisation within the field of ophthalmic surgery and this has created a climate in which further advances occur more rapidly. Cataract surgery is the most frequently carried out operation in ophthalmology and this has been changed forever by the introduction of intraocular lenses. No longer is the patient handicapped by the use of thick post operative aphacic spectacles, but now full visual rehabilitation is possible. The credit for developing intraocular lenses goes to an English ophthalmologist, Harold Ridley,



Dr Fitzsimons

Michael Delaney
MB BS FRACO FRACS

Ross Fitzsimons
MB BS FRACO FRACS

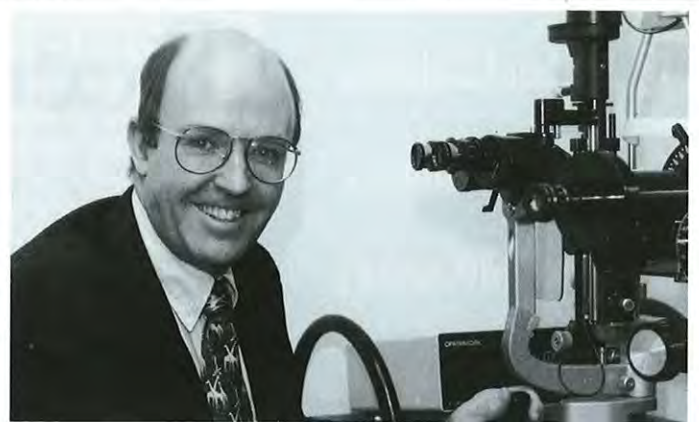
Peter McCluskey
MB BS FRACO FRACS

Dr T Justin Playfair
MB BS FRACO FRACS

Consultant Ophthalmologists



Dr McCluskey



Dr Delaney

who noticed that perspex chips retained in the eyes of fighter pilots during the World War II caused no reactions. He first developed intraocular lenses in the 50s but due to the lack of modern manufacturing techniques they were a failure. With time these problems were overcome and now it is routine to insert an intraocular lens into the lens capsular bag in the posterior chamber following cataract surgery. Intracapsular cataract techniques where the whole lens was removed were replaced by extracapsular techniques in the early 1980s and then by Phacoemulsification small wound techniques in the 90s. St Vincent's Clinic and St Vincent's Hospital were among the first of the major teaching institutions to introduce and teach Phacoemulsification techniques.

Refractive surgery is changing the concepts of what can be done to change the function of the eye. The Excimer laser used in the treatment of myopia is the result of extensive laser research and development for military and industrial purposes in the 80s. The benefits of this research are now being felt in all aspects of ophthalmic medicine and surgery.

ADVANCES IN SURGERY IN THE ANTERIOR SEGMENT

1) Cataract Surgery:

Phacoemulsification small wound techniques have revolutionised ophthalmic surgery. The standard wound in the eye is now between 3.2mm - 5-1/2mm and the wound is constructed in a self sealing technique so that in many cases sutureless surgery is possible. Apart from the obvious structural advantages to the eye of having a smaller wound, one of the

major advantages of the small wound is that they are astigmatically neutral. This means that following surgery to remove a cataract through a properly constructed wound the eye does not change shape, or the change in shape is minimal. One of the main disadvantages of previous techniques was that the large wound caused the eye to significantly change shape following surgery resulting in significant astigmatism. This astigmatic change interfered with the quality of vision following surgery and prevented full visual rehabilitation. With the new techniques, this effect is minimised allowing rapid visual rehabilitation with clear vision often being possible within several days to a week, and spectacles prescribed within four weeks of surgery.

Phacoemulsification technique involves the use of a piezo electric hand piece which generates ultrasonic energy to break up the lens substance while fluid flowing into the eye is aspirated out through the hand piece taking the lens material with it: as shown in Fig 1 and 2

below. The critical development which allowed this technique to be successful was the development of the continuous circular capsulorhexis, which is a tearing of a round opening in the anterior surface of the delicate lens capsule, allowing the contents of the lens to be removed with greater safety. An intraocular lens is then inserted through the opening into the lens capsular bag. The use of super viscoelastic fluids has facilitated the protection of the cornea and these are also used to dissect adhesions within the eye in complicated surgery in the equivalent manner that blunt dissection is carried out in other surgery.

The development of intraocular lenses has been noted to have been the critical development in visual rehabilitation. The most commonly used lens at the present time is made of a high grade medical PMMA (Poly Methyl Methacrylate) with an optic diameter of 5.5mm. New foldable intraocular lenses

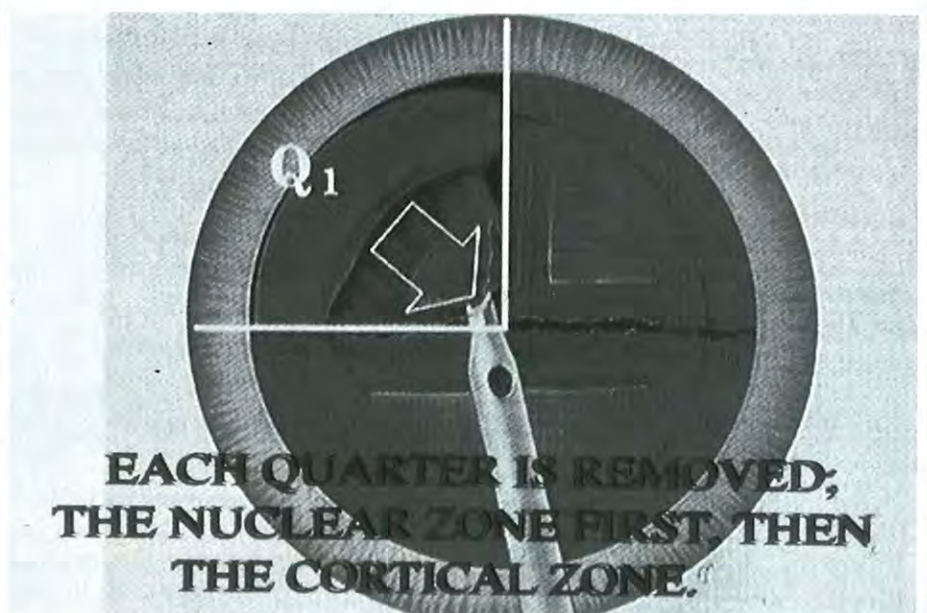


Figure 1

are being developed to allow insertions into very small wounds (3.2mm - 4mm). These lenses are truly marvels of modern technology where they can be bent and then resume their original state and still maintain extremely high quality optical surfaces and accurate powers. The advantages of these newer foldable lenses is the further reduction in size of the wound enhancing the advantages of the small wound discussed above. This process facilitates the rapid rehabilitation of patients who are able to resume their normal lives within a very short period of time following cataract surgery with minimal restrictions on their activities during their recovery period.

2) Glaucoma

Glaucoma surgery with the trabeculectomy operation has changed little over the last 20 years. The principle is to create a fistula to allow the aqueous fluid to drain in a controlled manner under the coatings of the eye and relieve the raised intraocular pressure. The main difficulty in this surgery is that the healing process often leads to failure with blockage of the fistula that has been created at operation. Recently anti metabolite drugs have been found to play a role in the prevention of closure of glaucoma fistularising operations. The use of these anti cancer drugs in the eye has significantly improved the outcome of glaucoma surgery. Five Fluorouacil and Mitomycin C are the two drugs used at

the present time with 5 Fluorouacil being routinely used in difficult cases.

Combined glaucoma and cataract surgery is now a well established technique and enables the patient to undergo one operation instead of a two staged procedure, and this is of obvious benefit to all patients. The use of Phacoemulsification cataract techniques has again increased the predictability of this operation and improved the outcome in terms of lowered intraocular pressure and better visual rehabilitation in these difficult cases. For intractable glaucoma an artificial valve has been developed. The Multeno valve is now inserted under the conjunctiva with a tube draining the anterior chamber to allow the reduction of the intraocular pressure in cases of intractable glaucoma.

3) Corneal Graft Surgery

Advances in corneal graft surgery have been mainly in the area of reducing post corneal graft distortion and astigmatism. It is always disappointing to have a successful clear corneal graft, but poor vision due to post transplant distortion of the graft. In line with other changes in ophthalmic surgery increasing attention has been paid to adjusting the shape of the eye and reducing the post operative astigmatism and distortion, especially irregular astigmatism. Better corneal trephines with improved suturing techniques allow post operative wound manipulation by the adjustment of the tension on the sutures to promote more rapid visual

rehabilitation. Improved eye banking techniques with longer storage times of donors allow better planning of the time of surgery to benefit the patient and their family. Astigmatic refractive surgical techniques are now used frequently to correct significant amounts of post operative astigmatism that were untreatable in the past.

The use of the Excimer laser to carry out phototherapeutic keratectomies (PTK) has enabled a number of patients to be treated as Outpatients, whereas in the past they underwent lamellar or penetrating corneal graft surgery. The Excimer laser ablates the superficial layers of the cornea, and this is discussed below. In PTK surgery this is done as a therapeutic rather than a refractive procedure. A number of chronic corneal problems which give rise to significant discomfort and visual impairment can be treated in this way. Superficial dystrophies such as Reis Bucklers dystrophy, recurrent corneal erosions and band keratopathy have all been successfully treated: as shown in the photos, Fig 3 and 4.

4) Refractive surgery

Refractive surgery is one of the rapidly expanding fields in ophthalmic surgery. Initially controversial it is now an accepted part of ophthalmology. Astigmatic keratotomy (AK) involves incisions in the cornea to correct significant amounts of post operative astigmatism. Techniques have been developed from those used in association with radial keratotomy for myopia and have been beneficial to post corneal graft and post cataract surgery patients. AK techniques involve small arcuate or tangential cuts in the steep axis of the cornea changing its shape and reducing the amount of astigmatism in that particular plane resulting in a more spherical cornea. The result is a better quality image and improved visual rehabilitation. Astigmatic keratotomy can also be used in association with refractive surgery for myopia increasing the number of patients who are suitable for modern Excimer laser surgery for myopia.

Several members of the Eye Department of St Vincent's Clinic are involved in treating patients with the Excimer laser for myopia. The technique involves using a laser in the UV spectrum at about 193 NM. This produces photons which break the



Figure 2



Figure 3: Band Keratopathy – pre PTK

carbon bonds resulting in a very accurate ablation of the cornea without mechanical or thermal injury during the photo refractive keratectomy (PRK), as shown in the slide of a human hair, Fig. No 5, which has undergone a PRK with an Excimer laser. The laser shaves four microns off the cornea with each pulse resulting in a flattening of the anterior surface of the cornea and reducing the myopic refractive error. Fig. No 6 shows experimental work where the cornea has been ablated as is seen by the concentric rings, but in this case a central island of tissue has been deliberately left to show that the corneal tissue has been ablated. Second generation Excimer lasers can now correct moderate amounts of astigmatism as well as myopia in the same procedure. These new lasers also increase the range of myopia which can be accurately treated to well over six dioptres of myopia which had previously been considered as the upper limit at which consistently reliable results could be obtained. Another advantage the new generation of Excimer lasers has over the old is an increased predictability of outcome of treatment with less corneal haze and more rapid visual recovery. New research has been carried out into the treatment of hypermetropia, and this is at the stage of clinical trials but is not clinically applicable at this time.

ADVANCES IN STRABISMUS SURGERY

Strabismus in children and adults is an important problem for four reasons -

firstly, an indicator of serious ocular or systemic disease, secondly as a cause of amblyopia in children, thirdly as the cause of double vision in adults and finally, but importantly, as a significant psychosocial disability. Treatment centres around adjustments of the twelve extraocular muscles through weakening and strengthening the corresponding pairs.

In recent years two significant refinements to the standard surgical approach have evolved.

a) Adjustable sutures

The use of fine, high strength sutures and microsurgical technique allow for the adjustment of extraocular muscle position post-operatively under topical anaesthesia. This has enormous advantage in achieving accurate ocular position and minimising the need for

subsequent surgery. Muscle adjustment is performed with patient co-operation within the first 24 hours after surgery.

b) Botulinum toxin injection

Now used for many indications by various specialties, this well known neurotoxin was originally developed as an aid to strabismus surgery by an ophthalmologist. The drug, when injected under EMG control, into an extraocular muscle, causes a flaccid paralysis lasting up to three months. This causes a shift in the ocular position and in certain situations, a permanent correction of the squint. It is injected under topical anaesthesia, as an out-patient, and has selected application where standard surgical techniques are not suitable.

Both these procedures have contributed significantly to our ability to relieve the dysfunction and disfigurement of strabismus.

ADVANCES IN POSTERIOR SEGMENT SURGERY

Closed Eye Surgery (CES)

The safe removal of vitreous haemorrhages associated with cerebral aneurysms, of non-metallic foreign bodies such as brass and certain sight threatening complications of diabetic retinopathy became possible with the introduction of closed eye surgery some twenty-five years ago.

CES utilises the natural optical properties of the eye. The microscope



Figure 4: Band Keratopathy – post PTK

can focus to any depth in the eye including the retinal surface as the cornea is made into a plane mirror by a contact lens. Additional light enters the eye by a light pipe and various instruments such as various cutters, forceps and scissors are passed into the eye through the pars plana, a 4mm strip of non-retinal tissue. The vitreous is aspirated into a hole at the end of the cutter and a guillotine within the cutter cuts the vitreous, and the vitreous haemorrhage, for example, is thus removed (vitrectomy). However, the volume hence the shape of the eye is maintained by fluid entering from a bottle through a separate site in the pars plana. Vitreous is not replaced, but rather the posterior segment which is now filled with infused fluid exchanges over a few days with normal ocular fluids. This vitrectomy operation is carried out with direct visualisation and third dimensional vision.

RECENT ADVANCES IN CLOSED EYE SURGERY

Perfluorocarbon liquids

These fluids are heavier than water. Intraocular lenses and sometimes fragments of cataract fall towards the posterior area of the retina. Fortunately, these objects can now be floated forward on these fluids and may then be readily removed.

Most retinal detachments are due to spontaneous tears in the retina and are treated by conventional surgery. However, with giant retinal tears the retina may fold upon itself like a pancake. Such detachments are now readily replaced by these heavy fluids. As the posterior part of the eye is filled the retina unfolds towards the anterior part of the eye. At the end of the operation the heavy fluid is replaced by either infusion fluid, special ocular gases or silicone oil.

Haemorrhages associated with macular degeneration

Macular degeneration associated with increasing age makes up to 50 per cent of the patients who are legally blind. Unfortunately in some, this blindness can come on overnight due to haemorrhage under the macula (the

reading area). If the haemorrhage is massive it may be possible to remove the clot with forceps, having made an incision through the retina posteriorly. In lesser degrees of subretinal haemorrhage the enzyme tissue plasminogen activator (TPA) is injected under the macula. After 45 minutes the clot should have dissolved and may be washed out.

Spontaneous holes in the macula

Macular holes occur with increasing frequency with aging. The patient becomes aware over a variable time that the vision from one eye is blurred and distorted. Examination reveals a circular absence of retinal tissue at the macula. This is often associated with a small localised retinal detachment. Unfortunately, in up to 10 per cent of cases macular holes occur in both eyes.

Some of these eyes may now be repaired by CES. A thin layer of surface vitreous is aspirated and then peeled off the retina, as if peeling a stamp off an envelope. A drop of blood, or serum or tissue growth factor is placed within the hole as a seal. The eye is then filled with an ocular gas and then the unfortunate patient is asked to lie face down for two weeks.

Most CES is concerned with removal of blood and scar tissue together with re-attaching of retinae. Injured and diabetic eyes comprise many cases. It is hoped soon to be able to renew visual function in that large group of older patients now suffering from macular degeneration or inherited diseases such as retinitis pigmentosa. Research is underway to enable a culture of retinal pigment epithelial cells to be placed under the retinal tissue.



Figure 5: Excimer Laser to human hair



Figure 6: Excimer Laser to a cornea

ADVANCES IN THE MANAGEMENT OF INFLAMMATORY DISEASE

Inflammatory eye disease encompasses a diverse range of entities which may involve either the ocular surface in diseases such as Sjogren's syndrome, peripheral ulcerative keratitis, episcleritis and scleritis, or the interior of the eye in diseases such as uveitis and retinal vasculitis. The inflammatory eye disease unit was established in 1984 as a collaborative clinic with the Department of Immunology and has managed in excess of 700 patients over the last 10 years.



SLIDE A: Infectious posterior uveitis caused by *Toxoplasma gondii*. This is treated with specific antimicrobial drugs such as sulphadiazine and pyrimethamine

St Vincent's Clinic provides a consultative service for patients with all types of inflammatory and immune mediated eye disease. Most patients are referred by other ophthalmologists for further investigation and treatment of severe sight threatening ocular inflammation. This usually requires systemic immunosuppressive therapy and these patients are managed jointly by both an ophthalmologist (PMc) and an immunologist (DW) using a variety of drugs.

A small number of patients have ocular inflammation which is clearly infectious (slide A), while the remainder have either idiopathic disease or inflammation associated with systemic inflammatory or immunological disease. Chronic ocular inflammation is difficult to control and may be associated with vision threatening complications such as macular oedema, glaucoma and retinal detachment.

The major advances in the management of inflammatory eye disease have been the development of the team approach to the management of patients with severe disease requiring systemic evaluation and treatment and the use of new drugs and drug regimens to treat ocular disease.

Patients with multisystem involvement by diseases such as Wegener's granulomatosis, sarcoidosis and Behcet's syndrome benefit

from integrated management of all aspects of their disease. A detailed assessment of their ocular disease and a thorough general examination focussing particularly on subtle systemic manifestations of diseases recognised to be associated with ocular inflammatory disease and pretreatment potential for side effects from systemic immunosuppressive therapy. The combined clinic was designed to accomplish these goals and represents a significant improvement in patient care.

The rational management of chronic inflammatory eye disease requires careful assessment by history, examination and a limited number of appropriate investigations. Infectious causes of chronic uveitis are treated with antimicrobial therapy. The treatment of patients with non infectious chronic inflammatory eye disease is similar despite the diverse aetiologies. Local therapy is used where possible for uniocular disease and a conservative approach to the use of systemic therapy. Bilateral vision threatening disease usually requires systemic therapy.

Corticosteroids are the mainstay of systemic treatment. Patients with inflammatory eye disease usually require long term treatment and are at risk of significant side effects. New strategies such as the use of intravenous pulsed doses of methylpredniolone, and the identification and monitoring of patients at increased risk of side effects such as osteoporosis are utilised to minimise complications.

New drugs and new methods for using established drugs have resulted in better management of vision threatening disease. Cyclosporin A is a potent new selective immunosuppressive drug which is effective, has relatively modest side effects and is non oncogenic. It works synergistically with corticosteroids and combination therapy using corticosteroids and cyclosporin A is now the preferred immunosuppressive regimen for severe intraocular inflammation. Low dose oral methotrexate represents a new method of using an old drug and has rapidly become a useful treatment strategy for many situations. A large clinical experience with low dose methotrexate in rheumatoid arthritis has



SLIDE B: Severe necrotising scleritis associated with rheumatoid arthritis. This requires treatment with systemic corticosteroids and cyclophosphamide

shown it to be a very effective and safe therapy and it is now increasingly used for ocular inflammation. Pulsed intravenous corticosteroids and cyclophosphamide are another new form of therapy using well established drugs to control very destructive acute inflammation such as that produced by widespread necrotising scleritis (slide B).

Complications of inflammatory eye disease such as cataract, glaucoma, retinal detachment and ocular perforations may require surgical intervention. New surgical strategies including the use of pulsed immunosuppression to cover patients perioperatively and modified Molteno valve glaucoma surgery improved the outcome of patients with inflammatory eye disease who require surgery.

HIV RELATED OPHTHALMOLOGY



SLIDE C: CMV retinitis in a patient with AIDS. This retinitis requires life long treatment with ganciclovir or foscarnet which are virostatic for cytomegalovirus

St Vincent's Hospital has been at the forefront of treatment of patients with AIDS and the inflammatory eye disease clinic has been involved in the management of ocular problems associated with HIV infection since the beginning of the epidemic in Australia. Up to 40 per cent of patients with AIDS develop a severe potentially blinding retinal infection with cytomegalovirus (CMV retinitis) (slide C). A range of other opportunistic microorganisms may produce infections involving the eye in patients with AIDS including: varicella zoster virus, herpes simplex virus, toxoplasma gondii and microsporidia species also occur and may result in significant visual loss.

St Vincent's has the largest clinical experience of any unit in Australia and has managed over 250 patients with CMV retinitis. The unit has been involved in numerous clinical trials of new medications for the treatment of CMV retinitis such as oral ganciclovir and intravitreal ganciclovir. St Vincent's clinic is involved in screening patients at risk of developing CMV retinitis and the treatment of patients with ocular manifestations of HIV infection.

Minimally Invasive Orthopaedic Surgery

The successful use of the endoscope in Orthopaedics must rate with effective internal fixation, antibiotics and arthroplasties as the great advances of the 20th century. Not only has the arthroscope significantly decreased the length of stay in hospital thus reducing costs, it has enabled patients to return to work quicker and has permitted procedures to be performed with much less pain.

The first endoscopy of a joint was performed with a cystoscope in 1918 by Professor Kenji Takagi from the University of Tokyo. He also designed the first arthroscope which had a 7.3 mm diameter. It was illuminated by an incandescent lamp near its tip. It was difficult to use and there was a tendency for the lamp to break. He continued to develop the arthroscope and by 1931 had the diameter down to 3.5mm and attached a lens for magnification. Development was also occurring in the West and the first article appeared in 1921. In 1931, Michael Burman of the Hospital for Joint Diseases in New York City published his experience on cadaveric arthroscopies of the knee, hip, shoulder, wrist, or ankle, and elbow. He warned that arthroscopy not be used indiscriminately or to satisfy curiosity. His efforts to establish arthroscopy were not heeded. At the same time in Japan the development of the arthroscope continued by Dr. Watanabe, a pupil of Takagi. The rapid development of electric and optical technology helped Watanabe who developed the No. 21 arthroscope which had a 6.5 mm

diameter sheath, a wide angle, and a tungsten light source. This still had a problem with the power of the light source and breakage of the lamp. The first commercially available arthroscopes became available in 1972. This came about with the use of fibre optic technology which permitted a strong light source to be used away from the patient which decreased the local heat production and the risk of burns.

The first arthroscopic surgery was by Dr. Watanabe in 1955 when he performed a partial excision of pigmented villonodular synovitis. The use of the arthroscope in the West followed the visit of Dr. Robert Jackson to Watanabe in 1964. On his return to Toronto, he began to use the Watanabe No. 21 arthroscope. After the introduction of the use of fibre optics the use of the arthroscope led to an explosion of interest by the orthopaedic community. In 1968 there were only 13 surgeons in the United States and Canada who had used the arthroscope. By the early 1980's over 98% of orthopaedic surgeons used the arthroscope. The first motorised shaver was produced by Johnson in conjunction with Dyonics in 1976. The use of a video camera attached to the arthroscope has made it easier for the surgeon to reach all areas of the joint, it enables an assistant to help and has permitted records of the findings to be made. The latest cameras are very small and of a very high resolution.

The modern arthroscope uses a fibre optic light source generally connected to a quartz iodide light source. This need to

Dr Brett G. Courtenay
MB, BS, FRACS, FA Orth A
Chairman,
Orthopaedic Department

be connected to a video camera otherwise macular damage to the retina can occur to the operator. The scope commonly used has a very wide angle and the most common scope has a 4.5mm diameter. There are smaller scopes available down to the needle scope at 1.9mm diameter. However, the smaller the scope, the smaller the field of vision and the lower the acuity of the lens system. The use of the video camera and television monitor certainly requires surgeons to master new skills where they need to watch the monitor to determine where their instruments are placed. However once this is mastered, arthroscopy of all joints becomes relatively simple.

INDICATIONS AND USAGE OF THE ARTHROSCOPE

THE KNEE

Technique:

The procedure is usually performed under general anaesthetic as this affords sufficient muscle relaxation to move around inside the joint. Local

anaesthetic does not give adequate quadriceps relaxation. The use of spinal and femoral nerve blocks means that the procedure is difficult to do as a day only procedure, which is how the majority are now performed. There are 9 standard portals described for arthroscopy of the knee. Commonly, two or three are used. One portal, usually anterolateral, is used to introduce the arthroscope, the anteromedial portal is used to introduce the operating instrument. A superomedial or superolateral portal may be used for a separate inflow or outflow cannula. During the procedure the joint is distended so that all structures can be seen. Posterior approaches on the medial and lateral sides can be used for loose bodies and for doing synovectomies.

Meniscal surgery:

i) *Excision:* The use of the arthroscope is the treatment of choice. There is no meniscal tear that cannot be excised with the arthroscope. There is a wide array of instruments that are used that either cut or punch out pieces. They are able to cut in all directions, even backwards. In addition there are very fine motorised shavers that can reach all corners of the joint. Apart from the shorter hospitalisation there is a shorter recovery time to return to work. Also in recognition of the load bearing and stabilising function of the menisci, it

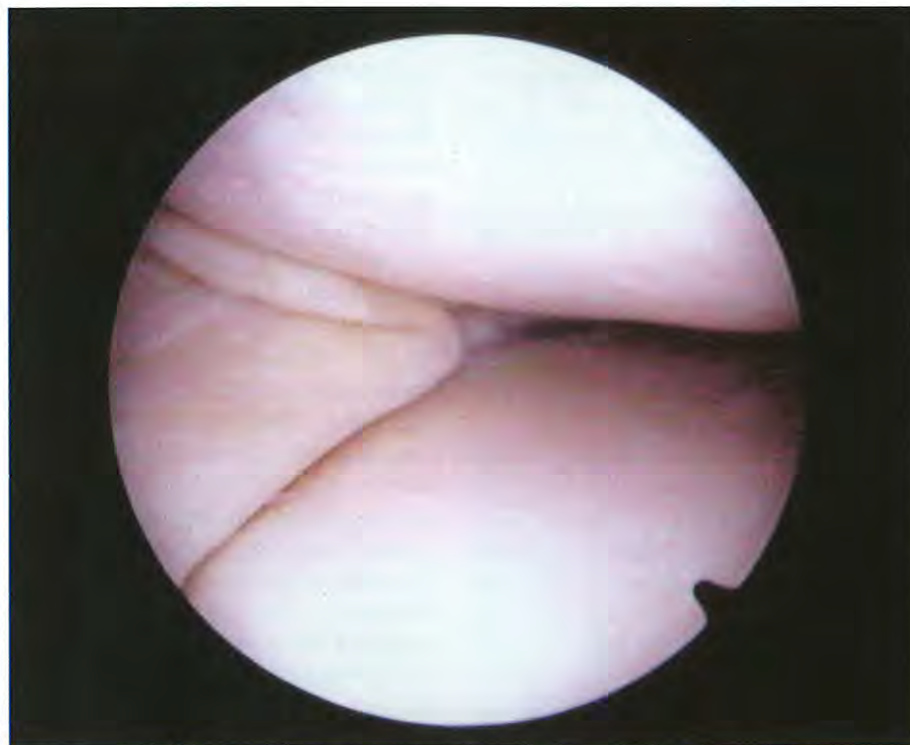


Figure 1: Tear of the posterior horn of the medial meniscus. There is limited access to this area, however, there are instruments designed to pass under the ends of the femoral condyles without damaging the articular surfaces



Figure 2: A patellar tendon transfer at twelve months after reconstruction

is possible to only perform a partial meniscectomy which should in the longer term decrease the effects of a total meniscectomy. This is difficult to prove as the results of meniscectomy are proportional to the state of the articular surfaces and the stability of the joint.

ii) *Repair:* In certain situations it is possible to repair the meniscus. As early as 1936 King showed both that the amount of degenerative changes in the joint after meniscectomy were related to the amount of meniscus that was removed and that in certain circumstances a meniscal tear would repair itself. Arnoczky and Warren have demonstrated the blood supply of the meniscus and with studies in immature canines have confirmed the repair of the meniscus. The younger the patient and the more peripheral the tear, the better the ability to obtain healing. The most successful repairs are those performed in association with an anterior cruciate ligament reconstruction within 8 weeks of the original injury. In these the success rate is about 90%.

Ligament Surgery:

The arthroscope is now used to assist in the placement of the ligament reconstruction in just about all situations. This permits smaller incisions to be used with less post operative pain. The technique is demanding as the view on the television monitor is only two dimensional. Accurate jig systems are therefore needed for correct placement of the drill holes. The time in hospital has been reduced from about 10 days only a decade ago to an average of about two days. It is possible to do these procedures as day only in certain situations. However as a patient is best

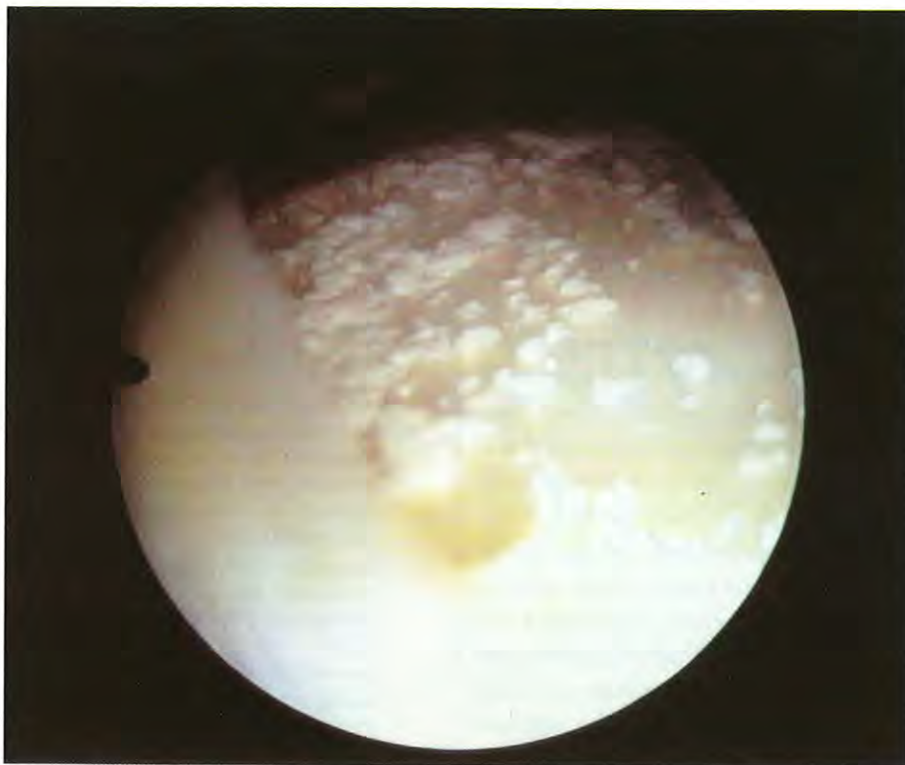


Figure 3: Gouty deposits in the articular cartilage. The arthroscope permits direct visualisation of the joint so that accurate determination of damage can occur

analgesed with parenteral narcotics at least for the first night this presents a problem. Medically however there is no contraindication to the patients going home. In fact many patients not in a health fund seem to manage very well; the analgesic effect of additional hospital costs!

Osteoarthritis:

The place of the arthroscope in osteoarthritis is best limited to those patients where there is not a major malalignment of the limb and a strong mechanical component to their symptoms. Lavage of the joint is a useful procedure but has a less predictable outcome as compared to when a debridement is performed. Success rates for arthroscopic debridement vary between 50% and 67% depending upon many factors, including the age of the patient, the alignment of the limb, degree of arthritis, activity level of the patient, and the extent of the follow-up. Lavage success rates are between 45% and 51%.

Other procedures:

Surgery on the articular cartilage can also be performed. At present this is limited to pinning back osteochondral

fragments and removing loose pieces of articular cartilage. In the very near future there will be agents that will be able to stimulate regrowth of articular defects and the arthroscope will be an ideal instrument to permit these procedures. In patients with patella problems, ligament reinforcements and releases can also be performed. Arthroscopy is also the means for removing loose bodies and foreign bodies, doing synovial biopsies and using powerful shavers, synovectomies.

THE SHOULDER

This is the second most frequently arthroscoped joint. The patient is usually placed on the side allowing access to the front and the back of the shoulder joint. The surgeon stands behind the patient and introduces the scope through the posterior portal. An anterior and superior portal can also be used for fluid inflow and for introducing other instruments. The joint is irrigated with an ampoule of adrenalin introduced to the fluid. This facilitates the view as there is a very good blood supply around the shoulder and of course a tourniquet cannot be used.

Surgery:

Loose bodies and articular cartilage defects can be dealt with such as in the knee. In addition, tears of the shoulder labrum can be debrided. Tears of the capsule associated with shoulder instability can also be seen as can complicated instabilities. At this point in time the success rate of arthroscopic repair of an unstable shoulder is not as good as can be obtained by open means when success is measured by the patient returning to strenuous sport. Extensive work is continuing however, and there will be improvements in the future.

Sub acromial Space:

This space can be entered by the arthroscope and after expanded with fluid and removal of the bursal tissue a good look at the rotator cuff from above and the overhanging acromion from underneath can be obtained. With the use of a mechanical burr a partial acromionectomy can be performed and small tears of the rotator cuff can be repaired. However many surgeons, after identification of the pathology, use a limited approach and do the acromionectomy through an open incision and also repair the rotator cuff this way. Again with improvements in instrumentation this will ultimately be done closed.

OTHER JOINTS

For many reasons, but primarily because other joints do not have as many complex soft tissue components these are arthroscoped less frequently. However as a means of assessing the articular surfaces, removing loose bodies and performing procedures on the articular cartilage there is no better means. The other common examined joints are the wrist, elbow, ankle, and hip.

RESULTS

The results of the procedures are very much related to the procedure being performed and the state of the articular cartilage. If there is no articular cartilage damage and the joint is stable the patient should be back to full activity in six weeks for simple procedures. More

complex surgery is obviously a product of what was performed. Patients however look at the puncture wounds and suspect that all arthroscopies are the same.

COMPLICATIONS

Complications are thankfully rare, but do occur. Infection is the most common serious problem. Septic arthritis occurs in about 1 in 1500 to 2000 procedures. Nerve and vascular injuries are more common around the shoulder and elbow. They are rare and are generally transient. Damage to the articular surfaces can occur in stiff joints and with less than ideal equipment. Fortunately these defects do not progress. A small number of patients develop pain in the back of the calf that raises the possibility of a DVT. Even though a DVT can and does occur, many of these patients suffer from extravasation of fluid from the back of the knee joint into the popliteal fossa. This is more likely to occur in a patient with a tear of the posterior horn of the medial meniscus and mimics a rupture of a popliteal cyst. Some patients develop a nodule at one or more of the entry portals. This is due to a small amount of fat necrosis either from the fat pad or direct contusion from the instruments. It

settles in a couple of weeks. Overall arthroscopy has the lowest complication rate for any procedure of similar complexity.

THE FUTURE

There will be continuing improvement in the instruments at our disposal. There will be better techniques for suturing inside the joint as well. Laser has been used but it is complicated and at this point in time does not offer any advantages to currently used methods. However this is sure to change. In the not too distant future there will be humoral mediators developed to reactivate the dormant chondrocytes and repair articular cartilage. As they will most likely need to be applied locally there will be an increased demand for the use of the arthroscope. Also with the pressure for decreasing medical costs and patients wishing to return to normal activities and work faster there will remain pressure on expanding minimally invasive surgery. One of the references used for this article talks of the dedicated arthroscopic surgeon. I believe that this is a throw back to the time when the techniques were being developed and there will not be such a person in the

future, all surgeons will be using the arthroscope either alone or in conjunction with open techniques. The principle will be less invasive surgery without sacrificing vision and results.

REFERENCES

1. Arnoczky SP, Warren RF: Microvasculature of the human meniscus. *Am J Sports Med* 10:90, 1982
2. Arnoczky SP, Warren RF: The microvasculature of the meniscus and its response to injury: An experimental study in the dog, *Am J Sports Med* 11:131 1983
3. Bircher E: Die Arthroendoskopie, *Zentrabl Chir* 48:1460, 1921
4. Burman MS: Arthroscopy, the direct visualization of joints: An experimental cadaver study, *J Bone Joint Surg* 13:669, 1931
5. Cannon WD, Vittori JM: The incidence of healing in arthroscopic meniscal repairs in anterior cruciate ligament reconstructed knees versus stable knees, *Am J Sports Med* 20:179, 1992
6. DeHaven KE, Hales W: Peripheral meniscal repair: An alternative to meniscectomy, *Orthop Trans* 5:399, 1981
7. Gillquist J, Oretorp N: Arthroscopic partial meniscectomy: Technique and long term results, *Clin Orthop* 167:29, 1982
8. Jackson RW, Marans HJ, Silver RS: The arthroscopic treatment of degenerative arthritis of the knee, *J Bone Joint Surg (Br)* 70:332, 1988
9. Johnson LL: *Arthroscopic Surgery*, Mosby - Year Book Inc. 1986
10. Johnson LL: *Diagnostic and Surgical Arthroscopy of the Shoulder*, Mosby - Year Book Inc, 1993
11. King D: The healing of semilunar cartilages, *J Bone Joint Surg* 18:333, 1936.
12. King D: The healing of semilunar cartilages, *J Bone Joint Surg* 18:1069, 1936
13. Kreuzer PH: Semilunar cartilage disease: A plea for the early recognition by means of the arthroscope and early treatment of the condition, *Ill Mes J* 12:290, 1925
14. Metcalf RW, Coward DC, Rosenberg TD: Arthroscopic partial meniscectomy: A five year follow up, *Orthop Trans* 7:504, 1983
15. Scott WN: *Arthroscopy: Past, Present, and Future*. In *The Knee*, Mosby - Year Book Inc. 1994

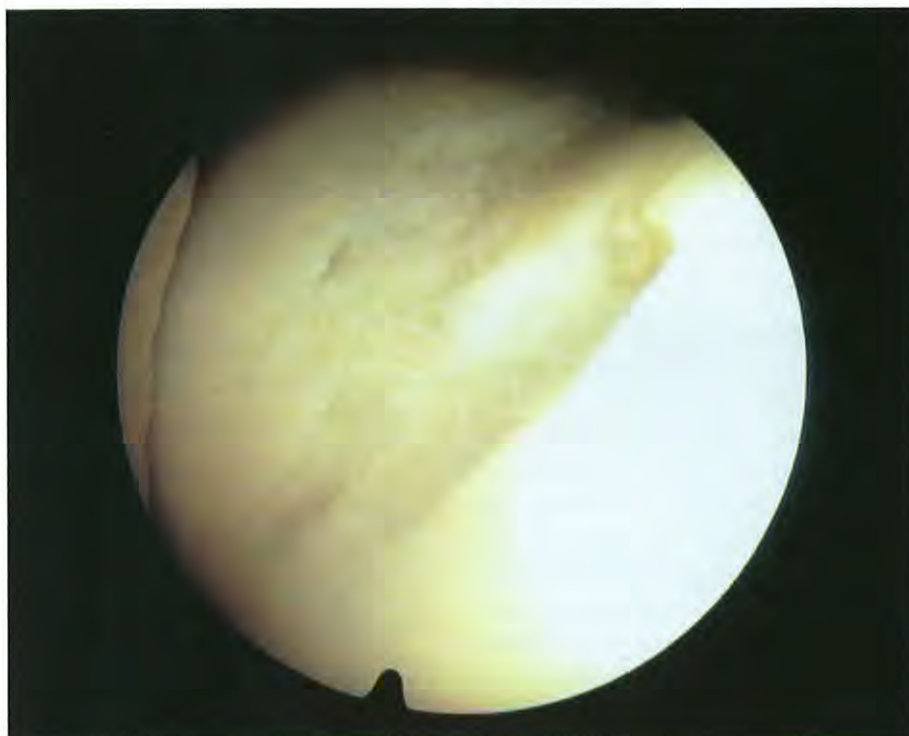


Figure 4: An isolated articular defect in the front of the femur in the area of articulation with the patella. At present the only true options are removal of the loose articular cartilage. However in the future it is hoped that these areas will be able to be repaired

Breast Cancer Strategies for Care – Operable Disease

INTRODUCTION

Although breast cancer is the most common malignancy in Australian women, with approximately one in thirteen likely to develop their cancer by age 75, a majority of effected women will live out their lives without recurrence of disease. Each year in NSW there are 2,500 new cases of breast cancer diagnosed and 900 deaths.⁽¹⁾

Adequate, initial, loco-regional treatment is carefully selected with due concern for psycho-social issues. Where possible, permanent loco-regional control should be achieved with the initial treatment programme. Patients, with tumours exhibiting features that place them in a high risk category for recurrent disease are identifiable⁽²⁾⁽³⁾ and planned for adjuvant therapy with predictable survival gains.

Presented with a potentially life threatening illness, the diagnosis of breast cancer and the treatment choices offered, represent a major crisis in a woman's life. It is essential to gently guide the patient through this difficult decision making process while spending sufficient time to communicate adequate information and provide access to appropriate literature, and where needed, community support.

At St Vincent's Clinic, best therapy is provided within a multidisciplinary team with input to the patient from surgical, radiation and medical oncologists. The general practitioner, after making or suspecting the diagnosis,

initiates and coordinates care with other health care professionals.

After referral, the surgeon/oncologist usually is the focus of patient care with subsequent input provided by interprofessional consultation.

SCREENING AND DETECTION

Australian women in the 50 to 70 year age group are specifically targetted by National Programmes, for the early detection of breast cancer. International studies have demonstrated the effectiveness of mammography as a screening method, detecting breast cancer well before physical examination. Randomized trials have demonstrated a 25-30% reduction in mortality from breast cancer screening, with mammography⁽⁵⁾⁽⁶⁾⁽⁷⁾⁽⁸⁾. This reduction in mortality, provides compelling evidence that early diagnosis and treatment can avert metastasis. Breast cancer should not be considered a systemic disease in all patients. There is no firm evidence that screening reduces mortality in younger age groups e.g. women 40-50 years.

Using improved techniques for imaging, with minimal radiation exposure, xray screening has resulted in the detection of patients with smaller tumours, and less or uninvolved axillary nodes.

Mammography increases the detection of non invasive, especially



ductal, carcinoma-in-situ; up to 20% of breast cancer detected by screening is ductal carcinoma in-situ (D.C.I.S).⁽⁷⁾⁽⁸⁾

PREMENOPAUSAL CANCER – FAMILIAL PATTERNS

Although breast cancer incidence increases with age, approximately 25% of Australian women will develop breast cancer under the age of 50.⁽¹⁾ This group, with the greatest life potential, often present a difficult diagnostic problem with painful, lumpy breasts that vary throughout the menstrual cycle. They have radiologically dense breasts that are difficult to interpret, unless microcalcification is present as a malignant marker.

Familial breast cancer, responsible for less than 10% of breast malignancy, is strongly represented in this premenopausal group. A family history of bilateral, premenopausal breast cancer is especially associated with high risk development of malignancy.⁽⁹⁾⁽¹⁰⁾ In this group x-ray screening can be justified at a younger age – say ten years younger than the youngest family member with cancer.

The recent isolation and cloning of the familial breast cancer gene

(BRCA1), along with exciting advances in molecular genetics, represent changes to the understanding of the cause, spread and treatment of breast cancer.⁽¹¹⁾ Regulators of the cell cycle, as well as the role of tumour suppressor genes have been studied. Cyclin dependent kinase inhibitors, critical regulators of the cell cycle have been identified. p16, a tumour suppressor gene, is of importance in the pathogenesis of several tumours, including breast cancer, BRCA1 has been localised to the long arm of chromosome 17. Females who have a defective copy of the BRCA1 gene have approximately an 85% chance of developing breast cancer by age 65. Molecular mechanisms that lead to sporadic breast and ovarian cancer are probably different to those that cause heritable breast, ovarian and colon cancer. A second breast cancer gene, BRCA2, present on the long arm of chromosome 13, disposes both men and women to the development of breast cancer, without increased risk of ovarian malignancy.⁽¹²⁾

We now have a better understanding of molecular genetics as a basis for breast cancer development. When available, gene testing should assist in management particularly in the premenopausal age group. Prophylactic therapy, including mastectomy, should then have a logical basis.

In my own practice, the commonest Hereditary Syndrome is an association of breast cancer with colonic cancer, both occurring in a younger than expected age group. Ovarian and uterine cancer may also occur. Three different primary cancers have been detected in the one patient. A less common Hereditary Syndrome is the association of breast cancer, with leukaemia and soft tissue sarcoma.

DIAGNOSIS

Cytology

Fine needle aspiration cytology and core biopsy are office procedures that complement physical examination⁽¹³⁾⁽¹⁴⁾ and together with mammography and ultrasound, establish the suspicion of malignancy in most patients with breast cancer.

Diagnosis is confirmed by open biopsy. Oestrogen and progesterone receptors are routinely tested in all patients with breast cancer.

Impalpable Tumours

With mammographically (or ultrasound) detected impalpable lesions, the diagnosis is best established by using hookwire localisation, with specimen x-ray confirmation.⁽¹⁵⁾ Frozen section is seldom used unless, at the time of wire localisation, an obvious mass lesion is encountered. It is inappropriate to use frozen section for a patient with an x-ray detected area of microcalcification⁽¹⁵⁾.

Stereotactic, x-ray guided, fine needle biopsy of impalpable, solid tumours is a useful technique. One may avoid open biopsy for benign pathology or use this technique for effective pre-operative planning in malignancy.

Pre-Op Testing

For most patients, with operable breast cancer, pre-operative work up is confined to the history, physical examination, breast imaging, chest x-ray and simple blood tests. Bone scanning is not routinely performed and used only in patients with abnormal biochemistry, ie raised serum alkaline phosphatase, or borderline operable tumours. The clinical value of the tumour marker, Ca15-3, is yet to be determined. It is

commonly raised in stage III and IV disease and is useful in the diagnosis of recurrent cancer especially with bone, liver and lung metastases. ⁽¹⁶⁾⁽¹⁷⁾

PROGNOSIS

Certain prognostic indicators with breast cancer have been clearly established. The most important is a knowledge of the number of ipsi lateral, axillary lymph nodes involved with cancer. Most modern adjuvant programmes using chemo and/or hormonal therapy, and the selection of patients for post operative radiation therapy, are based on this information.

Clearly, axillary sampling provides insufficient information. Axillary dissection is routinely performed. ⁽¹⁸⁾

Patients with negative axillary nodes have an overall 75% 10 year disease free survival; those with 4 or more involved lymph nodes have a less than 50% five year disease free survival; those with more than 10 involved lymph nodes have a disappointing disease free survival. ⁽¹⁸⁾⁽²⁰⁾

Tumour size and peritumour lymphatic invasion are independent variables important in the prognosis and planning for breast adjuvant therapy. ⁽¹⁸⁾⁽¹⁹⁾⁽²⁵⁾

Histological grading is also useful, especially in large tumours with negative nodes.

OPTIONS OF THERAPY

Whether mastectomy is chosen for operable breast cancer, or breast conserving surgery with local excision and radiation therapy, a total axillary dissection is employed in patients with invasive breast cancer, except when limited by age or disability. With in-situ ductal disease, axillary dissection is not considered. For palpable in situ disease with wide spread malignant microcalcification, low axillary sampling may be performed.

It is accepted that survival will depend on tumour staging at the time of diagnosis. Adequate local control with

equivalent long term survival rates can be achieved by either breast conservation and whole breast irradiation or modified radical mastectomy, as the standard operative procedures, for most patients with stage 1 and stage 2 disease. ⁽²¹⁾ Radical mastectomy may be used where infiltration of pectoralis major is encountered.

For most women "the problem initially is not perceived as mastectomy, it is cancer." ⁽²²⁾

As well as disease free survival, in considering the outcomes of treatment, one cannot ignore the importance to the patient of local recurrence or new disease following conservative breast surgery. Many patients fear this outcome and even though ultimate survival may not be effected, face further local therapy viz mastectomy, with anger, often at their own decision. ⁽²¹⁾ Recurrence, requiring salvage mastectomy, of up to 12% at five years and 20% at eight years has been reported. ⁽²¹⁾

International studies reviewing the psychological impact of treatment have demonstrated some surprising results. Several authors reporting the impact of treatment and long term psychosocial adjustment favoured mastectomy over local excision and radiation therapy, all with emotional distress sequelae increasing over time. ⁽²³⁾⁽²⁴⁾

NON CONSERVATIVE TREATMENT

Reasons for recommending modified radical mastectomy in stage I and stage II disease include :-

- cosmetic - where the relationship between tumour size and breast size, especially in a centrally placed tumour, rules out local excision.
- multifocal - based either on histological findings or mammography demonstrating more than one tumour.
- extensive ductal carcinoma in situ (D.C.I.S.) - where more than 25% D.C.I.S. is present in the invasive tumour and D.C.I.S. occurs in surrounding ducts.

- extensive malignant type microcalcification present on mammography.

In young women, with lumpy breasts, who develop breast cancer, the follow up of the conservatively treated breast may be extremely difficult.

A strong family history in this group may also influence one to perform a mastectomy. Prior radiation therapy may preclude breast conservation.

The surgical technique in breast conservation is important, with careful planning of the incision for maximum cosmesis and placement of drainage tubes within the anticipated radiation therapy field. A separate incision is used for axillary dissection in most patients.

It is important that proper orientation and inking of the excised pathological specimen be obtained, so that planning for re-excision can be appropriately made, should the margins prove to be inadequate.

IN SITU CARCINOMA

The increased recognition of in-situ carcinoma presents a new problem, with best treatment options as yet undecided. One should distinguish between low and high grade in-situ ductal carcinoma. The extent of high grade (comedo) ductal carcinoma is accurately mapped by mammographic findings marked by microcalcification. The low grade micropapillary cribriform variety of in-situ ductal cancer is under represented by x-ray findings.

Where in-situ ductal carcinoma presents as a palpable mass, or with wide spread malignant micro-calcification, total breast treatment is required. Small areas detected by screening x-ray are capable of local excision. The addition of radiation therapy, to such excision, is controversial with clinical trials proceeding. Clinical trials using prophylactic Tamoxifen are currently in progress.

RADIATION THERAPY

All patients choosing breast conserving surgery are treated with post

operative radiation therapy to the whole breast. There may be a future sub-group of patients identified with unifocal tumours and low risk of recurrence, in whom selective deletion of radiation therapy is possible.

Following mastectomy, post operative radiation is not routine. Selected patients will require radiation therapy to chest wall, internal mammary and supraclavicular chain. Therapy reduces the incidence of local recurrence and possibly improves survival.⁽²⁶⁾ Patient selection is based largely on the knowledge of involved axillary lymph nodes. In addition, large breast tumours with close margins and/or peritumour lymphatic invasion and high histological grade may be included in a group for post operative radiation therapy.⁽²⁵⁾⁽²⁶⁾ The axilla is not irradiated unless gross extra capsular disease is found.⁽²⁶⁾ Placement of the irradiation field, to cover the internal mammary chain and minimise cardiac toxicity, may be assisted by the use of internal mammary scintigraphy.

All therapy has its side effects and radiation may result in pulmonary toxicity in a small number of patients.⁽²⁷⁾ Classical radiation pneumonitis is a dose related toxicity and should be minimised with modern techniques. A small group, approximately 10% of all patients, develop bilateral sporadic pneumonitis which may have an allergic basis.⁽²⁸⁾ Patients who have severe pulmonary disease may not tolerate this complication.

RECONSTRUCTION

Following mastectomy, breast reconstruction is usually delayed for six to twelve months. With in-situ disease immediate reconstruction is offered.

The best long term results are achieved using the patients own tissue, especially the rectus abdominis "tram" flap - in selected cases this may require a microvascular anastomosis.

In a personal series of two hundred consecutive patients offered delayed reconstruction after mastectomy, only 9% underwent reconstruction after informed discussion with plastic surgeons. The number may have been greater if immediate reconstruction was offered.

SYSTEMIC THERAPY

The results from adjuvant programmes, using systemic therapy with chemotherapy and/or hormonal therapy have been well documented, reducing the risk of metastatic disease and death.⁽⁴⁾

The annual risk of recurrence for stage 1 and stage 2 breast cancer is reduced by approximately 30% and the overall mortality by 17% when chemotherapy or hormonal manipulation with Tamoxifen and/or ovarian ablation, is appropriately used.⁽⁴⁾

- Node positive premenopausal patients are treated with combination chemotherapy (usually CMF).
- Node negative premenopausal patients, with large tumours and high histological grade are similarly treated.
- Node positive and negative post menopausal patients receive adjuvant Tamoxifen, where hormone receptors are positive.
- Post menopausal patients, who are receptor negative, may be considered for chemotherapy in high risk disease, if under the age of 65.
- Node positive (or high risk) premenopausal patients, with positive receptors, may be offered ovarian ablation as an alternative to combination chemotherapy. This formerly popular procedure, shows a long term survival advantage.

High dose cytotoxic therapy with autologous stem cell rescue is being investigated in women with high risk breast cancer, where more than 10 axillary nodes are involved. Therapy is given after standard adjuvant CMF and is followed by chest wall irradiation. It is known that up to 87% of women with breast cancer with more than ten involved axillary lymph nodes relapse within five years of diagnosis. Some good responses for metastatic disease have been observed with this high dose programme.

Adjuvant CMF, is rarely used to treat elderly patients because of the fear of toxicity. Benefits in trials, to date, have not been clearly established in this group. In the future it is hoped that we

can better combine the sequencing of radiation and chemotherapy, to maximise advantage for the patient.

SUMMARY

Reduction in mortality has been demonstrated with early detection from screening mammography. The magnitude of the protective effect of such programmes however depends very much on the intensity of the programme, the screening interval and the compliance rate of patients long term.

Breast conservation is possible in selected patients with stage I and stage II disease. The psycho-social impact of conservative versus radical treatment needs further evaluation. Breast reconstruction following mastectomy, unless performed as an immediate procedure, is only accepted by a relatively small percentage of women.

The majority of patients with breast cancer will survive their malignancy, some live a long useful life with known disease, especially where their recurrence responds to hormone manipulation.

The age adjusted mortality from breast cancer can be reduced by the use of systemic therapy in patients with operable breast cancer.⁽⁴⁾

REFERENCES

- (1) Cancer in NSW. Incidence and Mortality Statistics 1989. NSW Cancer Registry.
- (2) Multiparametric Prognostic Evaluation Of Biological Factors in Primary Breast Cancer. Spyrtos F, Martin PM, Hacene K et al. Journal Natl Cancer Inst. 1992; 84:1266-77
- (3) Prognostic Factors and Natural History in Lymph Node Negative Breast Cancer Patients. Arriagada R, Rutqvist L.E., Skoog L, Johansson H, Kramar A. Inst. Guistave- Roossy, Villejuif, France. Breast Cancer Res, Treat. 1992; 21:101-9
- (4) Early Breast Cancer Trials Collaborative Group. (EBCTCG). Systemic Treatment of etc. Lancet 1992; 339:1-15, 71-85.
- (5) Mammographic Screening and Mortality From Breast Cancer; The Malmo Mammographic Screening Trial. Anderson I, Aspergren K, Janson L. Br. Med. J. 1988; 297:943-948
- (6) Analysis of Breast Cancer Mortality and Stage Distribution By Age Factor. Health Insurance Plan clinical trial. Chu K, Smart C, Tarone R, J.N.C./ 1988;

- 80:1125-1132
- (7) Edinburgh Trial of Screening of Breast Cancer: Mortality At Seven Years
Roberts M, Alexander F.E., Anderson T et al. *Lancet* 1988; 2:411-416
 - (8) Update of the Swedish Two Country Trial of Mammographic Screening for Breast Cancer. Tabac L, Fagberg C, South M, Day N, Duffy S. *Radiol. Clin. North Am.* 1992; 30:187-210
 - (9) Practical Guide for Estimating Risk For Familial Breast Cancer Ottman R, King M, Pike M, Henderson B, *Lancet* 1983; 2: 556-558
 - (10) Bilaterality in Familial Breast Cancer Patients. Anderson D, Badzioch M, *Cancer* 1985 ; 56: 2092-2098
 - (11) A Strong Candidate For The Breast And Ovarian Cancer Susceptibility Gene BRAC1. Miki Y, Swensen J, Shattuck-Eidens D, et al: *Science* 1994, 266: 66-71
 - (12) Bulletin of the American College of Surgeons T>J> Eberlein Jan 1995 Volume 80 No1 :p 39-42
 - (13) Role Of Cytology In Management Of Lesions Of The Breast Strawbridge H, Bassett A, Fordos I. S. *Gyn Obster.* 1981; 152:1-7
 - (14) Role of Aspiration Cytology in the Diagnosis and Management of Mammary Lesions in Office Practice
Bell D, Haydu S, Urban J. *Cancer* 1983; 51: 1182-1189
 - (15) Minimal Volume Excision Of Non-palpable Breast Lesions
Gallagher W, Cordenosa G, Roberts J, A.J.R. 1989; 153:957-961
 - (16) Ca 15-3 And Breast Cancer
Antoine E, Kayitaline L, Shielmann M. *Rev. Med. Interne (France)* 1994. 1510 p 650-62.
 - (17) Evaluation of Ca. 15-3 Tumour Markers In The Diagnosis Of Breast Cancer. Pilot Study. Woytack J, Djiewulska, Bokiniac A et al. *Neoplasma (Czech Rep)* 1994; 4174 p 213-6
 - (18) Relation of Number Of Positive Axillary Nodes To The Prognosis of Patient With Primary Breast Cancer. Fisher B et al A N.S.A. Breast And Bowel Project Update
 - (19) Relation Of Tumour Size, Lymph Node States and Survival In 24,740 Breast Cancer Cases. Carter C.L. et al. *Cancer*, 63; 181,1989
 - (20) Axillary Micrometastasis and Macrometastasis in Carcinoma of the Breast. Attiyeh F, Jensen M, Huvos A, Fracchia A. *Surgery* June 1977 , 144:839-842
 - (21) Mastectomy Versus Breast Conservative Therapy In The Treatment Of Stage I And Stage 2 Carcinoma Of The Breast: A randomized trial at the NCI
Lichter A.S, Lippman M.E, Danforth D.N, et al Natl Cancer Inst. Beth USA *J Clin Oncology* 1992; 10:976-83
 - (22) "Mastectomy and Sexuality"
Cancer Forum, July 1984 P43-44
 - (23) Breast Conservation Versus Mastectomy and Distress Sequelae as a Function of Choice. Savdie M., Levy RB, Hersberman , Lee JK, Lippman ME, Angelo et al. *Journal of Clinical Oncology* 1989. Vol 3 :367-375
 - (24) Psychological Outcomes of Different Treatment Policies in Women With Early Breast Cancer Outside a Clinical Trial
Fallow Field LJ, Hall A, Magosbe GP, Balm M, *Br. Med. J.* 1990; 301: 575-580
 - (25) Lymphatic Invasion in Patients With Node Negative Disease Peritumour Ductal Carcinoma Chemank CG, Boacchi P, Andreola S, Del Viechiom, Veronesi P, Rilke FO *Cancer* 1992; 69:1396-1403
 - (26) Post Mastectomy Megavoltage Radiotherapy: The Oslo and Stockholm Trials Auquier A, Rutqvist L, Host H, Rotstein S, Arriagada R. *Inst Gvistare-Roussy Villejuif, France Eur. Cancer.* 1992; 28:433-7
 - (27) Longterm Radiation Complications Following Conservative Surgery And Radiation Therapy In Patients With Early Stage Breast Cancer. Pierce S.M., Recht A, Lingos T, et al, Harvard Medical School Boston Int. J. Radiat. Oncol. Biol. Phys. 1992;23:915-23
 - (28) Radiation and the Lung: a Reevaluation of the Mechanisms Mediating Pulmonary Injury. Graeme W. Morgan and Samuel N, Breit Int. J. Radiat. Oncol. Biol. Phys. 1995; 31, No. 2, :361-369
 - (29) ABCTCG, Systemic Treatment Of Early Breast Cancer By Hormonal, Cytotoxic Or Immune Therapy. *Lancet* 1992; 339:1-15S, 71-85
 - (30) Growth Factor - Supported Dose Requested adj. Chemotherapy in Breast Cancer with > 10 Positive Nodes
Sianni A.M., Bregui M, et al *PROC. A.S.C.O.* 1992; 11:60
 - (31) High Dose Combination Cyclo Phosphamide, Cisplatin and Carmustine with Bone Marrow Support as initial treatment for Metastatic Breast Cancer: 3-6 Year Follow Up Peters, W.P. et al. *Proceedings of Am. Soc. Of Clin. Oncol.* 1990;9.10 .

Dr David Byrnes
Dr Anthony Davies
Dr Paul Edwards
Dr Stephen Mistilis
Dr Chris Vickers

The Endoscopic Biliary Revolution



Left to Right: WA Davies, PD Edwards, CR Vickers (sitting), DJ Byrnes, SP Mistilis

INTRODUCTION

Examination of body cavities was initially restricted to direct viewing with assistance from mirrors and prisms. During the late 1940's attempts were made to look into the stomach using rigid tubes incorporating semi-flexible tips which transmitted an image by a system of prisms. It is doubtful, however, that these were of any clinical value except in those patients with gross lesions.

Forty years ago the use of multiple fine glass fibres to convey an image was discovered. Over the following two decades fiberoptic endoscopes became more useful ⁽¹⁾ with incorporation of controls to bend the tip in two planes, wider angle lenses, provision for biopsy forceps, suction and automatic air insufflation.

By the beginning of the 1970's endoscopes were sufficiently sophisticated to enable examination of the entire upper gastrointestinal tract and the colon. At this time cannulation of the ampulla of Vater had become a reality and, as experience and the design of accessories progressed, a revolution occurred in the treatment of pancreatobiliary diseases. Now any pancreatobiliary surgeon would find it difficult to practice effectively without the backup of an experienced endoscopic proceduralist.

Further development in the late 1980's led to the replacement of fiberoptics by microscopic video cameras using charged coupled devices (CCDs). This provided a high quality image of the target area displayed on a video monitor where the operative site could be viewed simultaneously by several

Dr DJ Byrnes FRACP
Dr WA Davies FRACP
Dr PD Edwards MD, FRACP
Dr SP Mistilis FRACP
Dr CR Vickers FRACP

Gastroenterologists

PROCEDURES PERFORMED PER CALENDAR YEAR

	1990	1991	1992	1993	1994	Total
Upper & Lower	118	522	594	836	990	3,050
Lower	522	1,637	2,023	2,270	2,315	8,767
Upper	587	1,715	1,538	1,784	1,864	7,488
Liver Biopsy	8	33	103	159	174	477
ERCP	31	206	280	333	275	1,125
TOTAL	1,266	4,133	4,538	5,372	5,618	20,907

Figure 1: Table of Endoscopic Procedures St. Vincent's Hospital

people acting as a team - an essential requirement for complicated endobiliary procedures.

ENDOSCOPIC PANCREATICO- BILIARY PROCEDURES AT ST. VINCENT'S

The first endoscopic cannulation of the biliary tree at St. Vincent's Hospital was performed in 1973. Approximately six thousand such procedures have subsequently been performed in the hospital and, since the opening in 1990, have become an almost daily occurrence in St. Vincent's Clinic [Figure 1]. It is now quite common-place for a jaundiced patient to have a consultation in the Clinic followed by a diagnostic endoscopic retrograde cholangiopancreatogram (ERCP), a sphincterotomy on the ampulla, extraction of an impacted stone and be discharged home the same day! At least half of the ERCPs performed in the Clinic are interventional involving sphincterotomies, extraction of stones, insertion of stents or biliary dilatations.

INDICATIONS FOR ERCP

- Known or suspected common bile duct calculi
- Diagnosis of obstructive jaundice
- Drainage of obstructed bile-duct (stones or malignancy)
- Diagnosis of pancreatic tumours

- Assessment of chronic pancreatitis
- Treatment of biliary fistula
- Diagnosis of unexplained abdominal pain
- Emergency treatment for cholangitis
- Diagnosis of biliary parasites (particularly associated with AIDS)

METHOD OF PERFORMING AN ERCP

When performing an ERCP the patient is fasted, sedated and a side-viewing video-scope is passed through the stomach to a position opposite the Ampulla of Vater where the bile and pancreatic ducts join and exit to the duodenum. A small plastic cannula is selectively manipulated into either the bile or pancreatic ducts, contrast is injected and x-rays obtained. If intervention is required various accessories [Figure 2] are used to cut the sphincter muscle, extract or crush



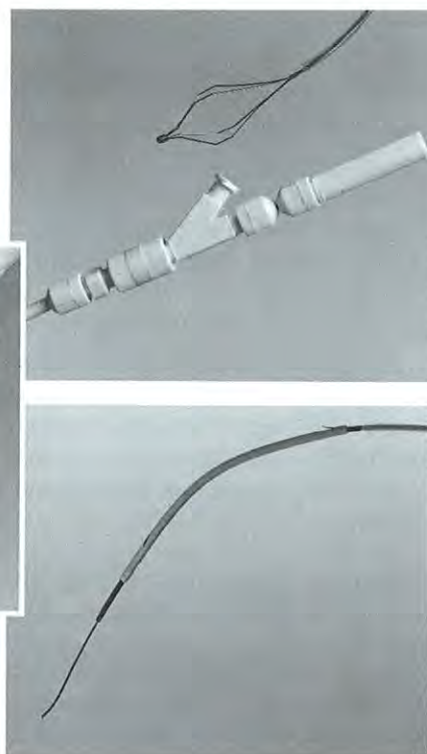
Figure 2: ERCP Accessories; Sphincterotomy Wire, Dormia Basket, Stent Set with Guidewire, Guiding Catheter, Stent and Pushing Catheter

stones, or guide plastic or metal stents through obstructing tumours. Depending upon technical difficulties the procedure may take from 10 to 90 minutes with the average being 15 to 20 minutes.

Unfortunately the procedure is not without risk and should **never** be performed by an **inexperienced** person as it is the only endoscopic procedure which carries a risk of death. Transient elevations in serum amylase are common after cannulation of the pancreatic duct with clinical pancreatitis occurring in approximately 3% of instances. Fortunately serious cases of pancreatitis are uncommon. Other complications include bleeding from a sphincterotomy, cholangitis after incomplete clearance of stones or failure to achieve drainage of an obstructing carcinoma, or duodenal perforation. The morbidity rate after endoscopic sphincterotomy for stone removal is 8% with a 30 day mortality rate of approximately 0.1%. However this risk is approximately a quarter of that associated with the alternative of surgical exploration of the common bile-duct.

COMMON BILE-DUCT STONES

An increase in the number of common bile duct stones being treated endoscopically is a direct result of the



move to laparoscopic cholecystectomy where exploration of the common bile duct, while possible, is not practical and virtually all common bile duct stones are now removed by endoscopic means either immediately before or after laparoscopic cholecystectomy ⁽²⁾ with open exploration of the common bile duct becoming a rarity. Giant stones can still provide a problem ⁽³⁾ but facilities are available for mechanical crushing of the stones and in some centres laser lithotripsy is used but is prohibitively expensive. For the very large stones patients at St. Vincent's Clinic are fortunate in having ready access to the renal piezo-electric lithotripter which is satisfactory for fragmenting common duct stones to a smaller size which can then be removed endoscopically. Overall, well in excess of 90% of common bile duct calculi can be removed endoscopically. The complications from endoscopic sphincterotomy and stone removal have been listed above.

MALIGNANT BILIARY OBSTRUCTION

It is now recognised that most pancreato-biliary malignancies are surgically incurable and palliation is the appropriate treatment. This used to involve a "triple bypass" (cholecysto or choledocho-enteric, gastro-jejunal and entero-enteric) with a thirty day mortality of about 30%. It is now routine to provide palliation from jaundice with endoscopic insertion into the biliary tree of plastic or metal stents ⁽⁴⁾⁽⁵⁾

A few patients still require a gastroenterostomy for duodenal obstruction but the incidence of surgery and suffering has been greatly reduced without any decrease in duration of survival. As well as stenting pancreatic or primary common bile duct tumours stenting is sometimes useful palliation in patients with hepatic metastases where a deposit has produced obstruction and jaundice by compression at the porta-hepatis.

Endoscopic stenting of malignant biliary obstruction is successful in about 85% of cases but this can be increased with a combined endoscopic-radiological approach (see later). The main problems encountered after stenting are stent



Figure 3: EWRCP in progress

obstruction which usually presents with a rigor followed by cholangitis and jaundice. Treatment of this condition requires urgent biliary decompression and it is often preferable to change plastic stents after 3 months in-situ to prevent this complication. Expanding metal stents provide longer patency (about 6 months) but are much more expensive and eventually occlude due to tumour ingrowth but this can be treated by placing a further metal stent inside the original stent. Later this year expanding metal stents which have a plastic covering to prevent tumour ingrowth will be available.

ASCENDING CHOLANGITIS

Pyogenic infection of the biliary tree usually occurs in association with biliary obstruction - almost always from calculus disease. It is a potentially fatal condition which can progress rapidly with septic shock and renal failure.

Antibiotics in this condition are usually ineffective unless the obstruction spontaneously resolves (stone disimpacts) or is relieved by intervention. A probable cause for antibiotics being ineffective in this situation is the demonstrated inability of the liver to excrete antibiotics into an obstructed biliary system.

Biliary drainage used to be established by surgery with considerable morbidity and mortality in a seriously sick patient. This risk is now circumvented by urgent ERCP with either a sphincterotomy and removal of common bile duct stones or by inserting a drain (stent) into the biliary tree. In this situation it is common to use a naso-biliary drain which is routed from the common bile duct to the exterior through the upper gastrointestinal tract and nose allowing flushing to ensure free drainage. This has proven to be dramatically effective for the emergency treatment of cholangitis although the mortality rate is still high if intervention is delayed until the patient becomes shocked.

ACUTE PANCREATITIS

It may appear paradoxical that ERCPs are sometimes performed at the height of an episode of pancreatitis but it has been demonstrated that patients with gallstone pancreatitis have a better outlook if the obstructing common bile duct stone is removed.⁽⁶⁾ Those patients who benefit most from the procedure are those who are critically ill and in whom the disimpaction is performed within the first 24-48 hours. Those with moderate or well established pancreatitis are unlikely to benefit from intervention.

The clues that pancreatitis may be induced by a common duct stone and therefore warrant an ERCP are:-

- gallstones demonstrated on ultrasound
- dilated common bile duct on ultrasound
- previous cholecystectomy for gallstones
- jaundice or cholestatic liver function tests
- absence of a history of alcoholism

CHRONIC PANCREATITIS

Patients with chronic pancreatitis sometimes have such disabling pain that surgical intervention is considered. However this is only likely to benefit the patient if a total pancreatectomy is performed (followed by numerous problems - particularly in the alcoholic), or an obstruction in the pancreatic duct is relieved. The best method to determine the latter is with a preoperative ERCP. Sometimes the examination precludes surgery by discovering and removing common bile duct gallstones, pancreatic duct calculi, stenting a pancreatic duct stricture or demonstrating a malignancy. Other times a dilated pancreatic ductal system suitable for a Peustow bypass operation is

demonstrated. However, in the alcoholic, the best results from intervention usually occur in those patients who stop drinking!

BILIARY FISTULA

Biliary fistulas used to be a serious complication of cholecystectomy. However insertion of a plastic stent into the common bile duct obviating obstruction by the ampullary muscle results in internal drainage [7, 8]. It has been our experience at St. Vincent's that the condition of such patients improves dramatically within 24 hours. After the fistula closes the stent is removed with an endoscope and snare.

TRENDS AND ADVANCES

1. Procedural success rate

Successful selective cannulation of the biliary or pancreatic ductal system is directly related to experience (and patience) although top quality endoscopic and x-ray equipment plus skilled nursing assistants are also important. Subtle changes in endoscope manufacture have made cannulation easier and this has been further facilitated by the use of controllable cannulas and super-slippery Teflon-coated guide-wires. Selective cannulation success

approaches 95-98% but frustrations still occur with anatomical obstacles such as duodenal diverticula (where the ampulla is frequently located within the diverticulum), by carcinomas and strictures precluding access to the ampulla or during acute pancreatitis where the duodenal mucosa may be so oedematous that the ampulla is obscured and the lumen so reduced in diameter that manipulation is impossible.

In those instances where cannulation has failed due to anatomical or pathological causes one can use a combined approach with an interventional radiologist where a bile duct is punctured by the percutaneous route and a guide-wire is passed down the common bile duct into the duodenum where it is picked up by an endoscopist and used to "railroad" accessories or stents up the bile-duct. This approach has been proven to be particularly useful in patients with malignant biliary obstruction where it has not been possible to pass a guide-wire from the ampullary end.

2. Commercial stents

The method for inserting biliary stents is now well established but gradual occlusion of the stent from accumulation of bacterial products on the inside of the stent remains a problem. It is customary to change 10F plastic stents about every 3 months to avert cholangitis associated with stent obstruction. An alternative (costly) to the plastic stent is an expanding metal-mesh stent which expands to approximately 1 cm in diameter after deployment. These stents usually remain patent for about 6 months but are eventually blocked by tumour ingrowth through the mesh. In this situation a further mesh stent can be passed through the original stent with re-establishment of drainage. It is believed that later this year a polythene covered metal-mesh stent will become available which will hopefully prevent obstruction by tumour ingrowth. There has also been experimentation with teflon stents and these may retain longer patency than the ordinary plastic stents.

Stents for pancreatic strictures have also been devised⁽⁹⁾ but the indication for their use, how long they should



Figure 4: Sphincterotomy with Stone

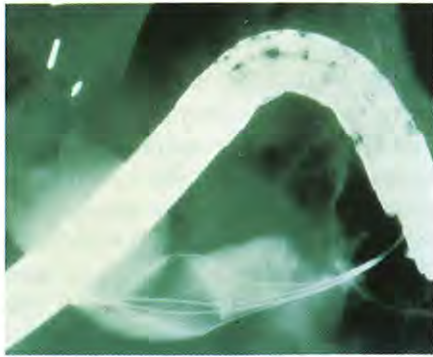


Figure 5: Removal of common bile duct calculus after cholecystectomy. Note lower stone trapped in dormia basket

remain in-situ and the difficulty of excluding malignant strictures has not been established and these are still rarely used.

3. Manometry

Some patients even after cholecystectomy and clearance of the common bile duct, continue to have biliary colic which is thought to be due to dysmotility of the ampullary sphincter ("biliary dyskinesia"). About half of these patients are cured by endoscopic sphincterotomy but in these patients (in whom the common bile duct is often not dilated) there is a 20% morbidity associated with the procedure. Attempts have been made to confirm the diagnosis of biliary dyskinesia by manometry of the ampullary sphincters but this carries a 25% risk of pancreatitis, is of limited clinical value and remains mainly a research tool.

4. Endobiliary Radiotherapy

Attempts have been made to irradiate biliary tumours by insertion of intraductal iridium wires. This has theoretical advantages but has problems of cost, availability and irradiation of staff with little interest being shown in the procedure.

5. Mother and daughter scopes

Miniature fibrescopes have been devised to pass down ERCP scopes allowing direct visualisation of the interior of the biliary tree. This could be useful for ensuring complete removal of calculi or for fragmentation of large calculi using pulsed dye laser. However the baby scope is largely destroyed by a single procedure and the cost precludes routine use.

REMAINING OBSTACLES

1. Cost

ERCPs, although very useful, are a high-cost exercise requiring highest quality x-ray equipment, expensive endoscopes, highly-trained staff, considerable time and often very expensive accessories eg each single-use sphincterotome, guide-wire or stone retrieval basket costs \$200 and frequently several of these are required for a single patient. Metal mesh stents cost approximately \$2000 but this can be recovered from Health Funds.

Due to the required expertise and high cost, ERCPs, with the exception of St. Vincent's Clinic, are almost only performed in Public Hospitals. In the latter situation cost constraints often restrict the number of procedures performed and the use of expensive accessories eg metal stents.

Paradoxically, in the private situation it is often easier to gain access to appropriate stents and single-use accessories as these expenses are at least partially covered by Health Funds.

2. Expertise

The success and safety of ERCPs is directly related to past and continuing experience. It is the only endoscopic procedure with a mortality rate and definitely should not be attempted

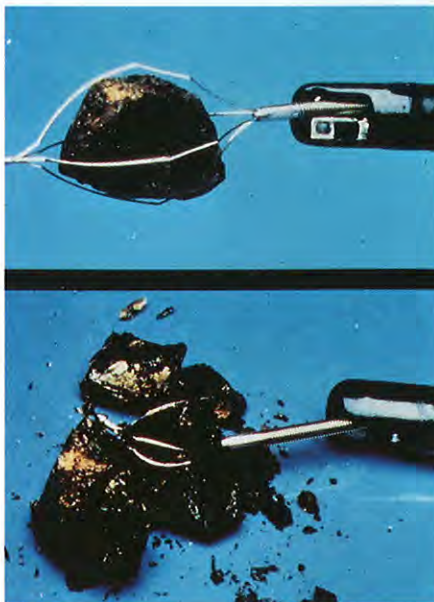


Figure 6: Fragmentation of large calculus by mechanical lithotripter

without the best of equipment, back-up resources and continuing experience.

3. Equipment

The video-equipment has become so refined that the picture is close to the resolution of the human eye making further improvement unlikely. Accessories have also been well designed and are able to cope with almost all clinical requirements. Thus it seems unlikely that there will be many significant advances in equipment in the future decades.

SUMMARY

In experienced hands and with appropriate indications interventional ERCP has proven to be a most valuable tool for the diagnosis and treatment of pancreato-biliary diseases. St. Vincent's Clinic is one of the very few Day Centres where these procedures are available.

REFERENCES

1. Hirshowitz BI: Development and Application of Endoscopy. *Gastroenterology* 1993, 104:337-342.
2. Mitchel SA, Jacyna MR, Chadwick S: Common Bile Duct Stones: A Controversy Revisited. *Br J Surg* 1993, 80:750-759.
3. Binmoeller KF, Bruckner M, Thonke F, Soehendra N: Treatment of Difficult Bile Duct Stones Using Mechanical, Electrohydraulic and Extracorporeal Shock Wave Lithotripsy. *Endoscopy* 1993, 25:201-206.
4. Davids PHP, Groen AK, Rauws EA, Tytgat GNJ, Huibregtse K: Randomised Trial of Self-Expanding Metal Stents Versus Polythene Stents for Distant Malignant Biliary Obstruction. *Lancet* 1992, 340:1488-1492.
5. Wagner JH, Knyrim K, Vakil N, Klose KJ: Plastic Endoprosthesis Versus Metal Stents in the Palliative Treatment of Malignant Hilar Biliary Obstruction. A Prospective and Randomised Trial. *Endoscopy* 1993, 25:213-218.
6. Carr-Locke DL: Role of Endoscopy in Gallstone Pancreatitis. *Am J Surg* 1993, 165:519-521.
7. Fouch PG, Harlan JR, Hoefler M: Endoscopic Therapy for Patients with Postoperative Bile Leaks. *Endoscopy* 1993, 39:416-421.
8. Mortensen J, Kruse A: Endoscopic Management of Postoperative Bile Leaks. *Br J Surg* 1992, 79:1339-1341.
9. Sacred ZA, Ramirez FC, and Hepps KS: Endoscopic Stent Placement for Internal and External Pancreatic Fistulas. *Gastroenterology* 1993, 105:1213-1217.