
WHAT'S NEW IN

Series Introduction - 'What's new in ...'

Series Editor Major JP Garner

Scientific advancement proceeds apace in all areas of medicine; it is within the lifetime of most of this Journal's readership that cardiac transplantation has progressed from a flawed experimental procedure to a routine treatment option for a variety of cardiac ailments. As the spectre of revalidation looms large each of us within the profession is beholden to 'remain current', whatever that may mean. It is clearly impractical, and irrelevant, for every practising doctor to know the intricacies of every advance in every branch of medicine; but a passing acquaintance with the 'Headline News' can often prove useful in

unfamiliar circumstances. Most military doctors are to some extent, by the very nature of the job, generalists and this series of articles is designed to provide an overview of the most recent advances in the various disciplines of medicine. It is written for a general readership and the specifics and technicalities have been omitted; interested parties may use the reference listings to direct themselves to relevant further reading. The first article in this series covers the recent advances in General Surgery, whilst future contributions will include general medicine, anaesthesia and plastic surgery.

What's new in ... General Surgery

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Introduction

It might be imagined that apart from the quantum leap in technology imparted by the arrival of laparoscopy and endoscopy, there is little scope to modify surgery that has stood the test of time over many decades. That is a consideration when thinking only of operative surgery and as all surgeons young or old will tell you, surgery encompasses much more than just operating – it is the management of surgical disease. Casting ones mind back to medical school, management of disease starts with diagnosis and runs through everything we do to the patient until we have finished treating them and viewed in this context there is enormous scope for changes and improvements in surgical practice. One prominent theme throughout this review of recent advances in the four major subspecialties of general surgery, is the contribution made to surgical management by non-surgeons, be they radiologists, oncologists or even robots. Some are already integrated into routine practice, others require further confirmatory trial results before evidence-based changes in surgical management can take place.

Vascular Surgery Screening for abdominal aortic aneurysms

Abdominal aortic aneurysm (AAA) is a common condition, affecting men more so than women. If left untreated it has a high risk of rupture which is associated with an overall mortality rate of 90%. Of those that

reach hospital alive and proceed to emergency repair, only 1 in 2 will survive. This compares poorly with a mortality rate of 3-10% for elective open aneurysm repair. The question of screening for AAA has been a vexed one, but two studies have reported in the last year that should effectively end the debate. The Multicentre Aneurysm Screening Study (MASS) group (1) have reported the results of a randomised controlled trial which enrolled over 65,000 men aged 65-74. Half were invited to attend for a screening abdominal ultrasound. Those with aortic diameters over 3cm were followed up for a mean of 4.1 years. Elective surgery was offered when the aneurysms reached standard criteria. There was a highly significant reduction of AAA-related death in the screened group of 42%, with over three times as many elective repairs performed than in the control group. The elective surgical mortality rate was 6%. Half the number of emergency AAA repairs were performed in the screened group compared to those not invited for screening. A secondary analysis of the data with regard to cost effectiveness demonstrated that at 4 year follow up, this programme was just acceptable to NHS cost standards. Cost effectiveness was predicted to improve substantially with longer follow up (2). A randomised trial from Denmark of 12,658 men aged 65-73 demonstrated a significant reduction in AAA-related death (6 versus 19 deaths) in the screened group (3). In comparison to these studies on men, it is notable that

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screening for AAA in women is ineffective. The Chichester randomised trial followed 9342 women aged 65-80 for up to 10 years and found no difference in the rate of rupture between the screened and unscreened group (4).

Conclusion: Men over the age of 65 should undergo a single screening ultrasound of the abdominal aorta.

Endovascular aortic aneurysm repair (EVAR)

Whilst not new, the first successful EVAR procedures were performed in 1991(5), it is timely to review the medium term results and current indications of this innovative approach to aneurysm repair. EVAR requires a detailed knowledge of the aneurysm morphology and the improvements in CT imaging have gone hand in hand with advances in endovascular therapy (Figure 1) (6). The long-term follow up of these patients is skewed somewhat by the technical failings of older stents. The original designs and techniques applied at the outset of EVAR are now recognised to be suboptimal. Consequently, early series describe an excessive rate of complications. This is elegantly demonstrated in a series from Germany (7) detailing a 6 year experience of EVAR. The conversion to open operation rate fell from 10.9% in the first year to 2.4% in the latter 5 years. The mortality rates in the two periods fell from 8.3% to zero. Two series, each trialing a new stent design, give similar promising medium term data. Abraham *et al* (8) describe a re-intervention rate for endoleak of 4.3% with no conversions to open surgery; there was one non-AAA related death within 30 days and one late AAA rupture. The second trial (9) describes a conversion rate of 3.3%, endoleak rate of 5.9% and one procedure related death out of 118 patients. There are now reports of successful endovascular treatment of recurrent (10) and mycotic AAA (11), thoracoabdominal aneurysms using multiple stents (12,13), traumatic thoracic aortic injury (14) and ruptured AAA treated under local anaesthetic (15).



Fig 1. 3-dimensional CT reconstruction of an abdominal aortic aneurysm. The infra-renal neck and the normal calibre vessel above the iliac arteries can be clearly seen.

Conclusion: In a well selected group of patients EVAR represents a less traumatic method of treating AAA with reasonable medium term results. Long term results from modern stent systems are needed from collaborative databases such as EUROSTAR (16) before endovascular treatment becomes routine. EVAR is not suitable for all aneurysms so there is a continuing need for open repair.

Carotid artery angioplasty and stenting (CAS)

It is estimated that 20-30% of cerebrovascular events are due to carotid artery occlusive disease and that surgery (carotid artery endarterectomy (CEA)) provides superior protection against strokes than best medical therapy. Endarterectomy does, however, have its own inherent risk of stroke, consequent upon embolization of the atherosclerotic plaque. Surgeons' penchant for minimally invasive therapy has now reached the carotid arteries with the introduction of CAS. It is being considered as an alternative in high-risk patients who are currently deemed too risky for open surgery. Initial reports are encouraging from single centre series but there are no published randomised controlled trials of CAS v CEA. Shawl (17) reports a series of 343 CAS procedures with major and minor stroke rates of 0.6% and 2.3% respectively at 30 days. At mean follow up of 26 months the re-stenosis rate was 2.7%, all of which were asymptomatic. A study from Germany (18) compared 100 CAS patients against a retrospectively reviewed group of 142 CEA patients and found no difference in complication rates (stroke, myocardial infarction, or death) between the two procedures (6.5% [CEA] v 8% [CAS]). Any potential benefits of CAS are dependent on achieving lower rates of stroke and death than CEA, so the study from Jordan *et al* (19) sounds a cautionary note. They compared the complications between high and low-risk procedures across a series of 415 endarterectomies and achieved an outstandingly low stroke rate (2%) with no difference between the high and low-risk groups.

Conclusion: Carotid artery angioplasty and stenting is a safe and technically feasible minimally invasive treatment for occlusive carotid artery disease. At present there is insufficient evidence to support its widespread adoption although it may be beneficial in high-risk patients.

Medical therapy for peripheral vascular disease

It is widely recognised that peripheral vascular disease (PVD) is only one manifestation of generalised atherosclerotic disease and that patients with PVD are at increased risk of stroke, myocardial infarction and early death. The recent

evidence points to aggressive lifestyle modification and pharmacological intervention as being vital to the long-term outcome of PVD patients. These drug interventions should include help with smoking cessation if necessary, statin therapy to control hyperlipidaemia (20) and anti-platelet therapy. The CAPRIE trial (21) randomised over 19,000 patients with symptomatic atherosclerotic disease to receive aspirin or clopidogrel as antiplatelet therapy. The clopidogrel group demonstrated an 8.7% relative reduction in the risk of ischaemic stroke, myocardial infarction or vascular death over 1-3 years, with the most marked benefit seen in the subgroup of patients with PVD. Additional studies have shown further benefit from taking aspirin *and* clopidogrel in prevention of acute vascular events (22) after acute coronary syndrome. It is reasonable to suppose that similar benefits might accrue in peripheral vascular disease patients. Aside from risk reduction in PVD there are new studies which detail good symptomatic benefit in intermittent claudication from pharmacological treatment. Pentoxifylline improves walking distance by about 25% (23) whilst a newer phosphodiesterase type III inhibitor, cilostazol, improves walking distance by between 40-60% (24) coupled with increases in high density lipoprotein concentrations and decreased triglyceride concentrations (25).

Conclusion: Patients with peripheral vascular disease usually have coexisting disease and are at high risk of other vascular events. They should receive aggressive medical management to reduce these risks.

Coloproctology

Laparoscopic colorectal surgery

Laparoscopic colorectal surgery is becoming increasingly popular due to its perceived benefits of decreased post operative morbidity, quicker return to function and reduced hospital stay, although in the UK its availability is still largely dependent on local expertise and enthusiasm. Current NICE guidelines state that laparoscopic colorectal resections should only be performed as part of a trial.

Laparoscopic colorectal surgery can be performed entirely laparoscopically such as laparoscopic rectopexy, or be 'laparoscopically assisted', where part of the procedure is carried out laparoscopically, such as the colonic mobilisation and mesorectal excision in a laparoscopic anterior resection, before specimen removal and anastomosis through a limited incision. For benign colorectal resection, there certainly appear to be benefits. Braga *et al* (26) recently report a randomised trial of laparoscopic versus open colorectal surgery in 269 patients, and found reduced morbidity (20% vs 38%), inpatient stay (10.4 vs 12.5 days) and tissue metabolic reaction to surgery in the laparoscopic group. A Canadian study (27) reported similar

findings in a randomised trial of 279 patients, with no differences in operative time, complications, morbidity or mortality. The laparoscopic group however, required less analgesia, resumed feeding earlier and had a shorter inpatient stay (7.7 vs. 11.0 days).

A common argument against the widespread adoption of laparoscopic colorectal surgery has concerned the adequacy of oncological resection in cancer surgery. A recent meta-analysis by Korolija *et al* (28) included 3935 patients and found similar results for open and laparoscopic surgery in terms of lymph node clearance and surgical margins.

Within the UK, laparoscopic colorectal surgery has largely been included in the MRC ClasicC trial since 1996, which finished recruiting in 2002 with over 800 patients enrolled from 27 centres. Short-term outcomes of intra-operative complications, post-operative complications and recovery times and oncological resection parameters have been similar in both groups. Long-term outcomes are awaited, although a survival difference would seem unlikely in view of the similarity of the oncological resections. For rectal cancers included in the ClasicC trial (381 cases) however, significant technical difficulties are reflected in a 34% rate of conversion to open surgery, and concerns have also been raised regarding autonomic nerve preservation during laparoscopic TME (29).

Conclusion: Laparoscopy in colorectal surgery appears to offer some benefits over conventional surgery without compromising oncological clearance, although considerable technical difficulties remain. It is hoped that the increasing number of specific laparoscopic colorectal training programmes will help to lower the conversion rate and further improve outcomes.

Advanced Colonoscopy

Advances in colonoscopic techniques, technology and teaching have moved colonoscopy into a new age as a therapeutic tool. Zoom endoscopes with up to 100x magnification, and improvements in endoscopic resection equipment have allowed the introduction of endoscopic mucosal resection (EMR). In this technique early tumours or neoplastic lesions are raised up on a bed of saline injected submucosally and precisely excised using diathermy, all performed via the colonoscope.

Since Kariya's (30) first case report in 1977, many Japanese studies have expounded the 'flat adenoma-carcinoma sequence' theory, suggesting that infiltrating colorectal cancers originate from flat lesions. Kudo *et al* classified flat adenoma crypt patterns seen at magnified chromoscopic endoscopy into five types, with types III, IV and V being at risk of malignancy (31). These flat lesions were initially considered to be

unique to Japan, but a 2000 study (32) showed a similar incidence in the UK when the same colonoscopic techniques were used. During 1000 routine colonoscopic examinations 321 adenomas were found, of which 63% were polypoid and 36% flat; amongst the adenomas 10% were severely dysplastic. The likelihood of Dukes' A cancer or severe dysplasia increased according to a morphological hierarchy (Table 1). 54% of lesions containing severe dysplasia or Dukes' A carcinoma were flat or depressed. Kudo has previously shown that although the incidence of flat adenomas is high it is actually the depressed lesions that progress to colorectal cancers and that treatment by EMR is optimal (33).

Chromoscopic colonoscopy uses two dyes, indigo carmine (blue) and crystal violet (purple). The indigo dye spray accentuates the borders of a lesion, making it easier to define, thereafter crystal violet is used to help identify crypt patterns, in conjunction with a magnifying colonoscope. Classification according to crypt pattern allows some assessment of neoplastic potential and selection of an appropriate treatment modality such as guided biopsy, EMR, or tattooing and endoclip marking for further surgical intervention.

Conclusion: Advanced diagnostic and therapeutic colonoscopic techniques are being adopted. These can lead to the early identification of colorectal lesions, potentially allowing less invasive treatment.

Stapled haemorrhoidectomy

The treatment of haemorrhoids has been revolutionized in 1998, by the introduction of the stapled haemorrhoidectomy (34), which uses a circular stapler to remove a circumferential cuff of mucosal tissue 2-4cm above the dentate line. At operation, a split proctoscope is inserted and a pursestring suture is placed 2-4cm above the dentate line. The stapling device is then inserted with its anvil above the pursestring, which is then tied; as the stapler is closed a cuff of mucosa is trapped in the stapling gun. The device is fired, removing this cuff of tissue, and stapling the edges together, thereby removing redundant mucosa, and interrupting local blood supply to haemorrhoidal tissue.

The first two randomised controlled trials of stapled vs. conventional haemorrhoidectomy were coincidentally published on the same date. Roswell and colleagues (35) found stapling reduced pain, time to return

to normal activities and hospital stay in their trial of 22 patients, whilst Mehigan *et al* (36) randomised 40 patients and found analogue pain scores significantly less in stapled cases (mean 2.1 vs 6.5) with a quicker return to normal activity (17 vs 34 days). In the largest trial to date, Ho *et al* (37) randomised 110 patients and found the stapled procedure to be less painful postoperatively, with less bleeding and pruritus ani.

Further studies in a similar vein continue to recruit and report. A large multinational randomised trial, the STOPP trial, comparing stapled haemorrhoidectomy with traditional Milligan Morgan technique is currently in analysis, and within the UK, the Association of Coloproctology of Great Britain and Ireland has an ongoing voluntary audit for all members to assess outcomes. Although the cost of the device makes the procedure-related cost higher, stapled haemorrhoidectomy may actually represent a cost saving to NHS trusts, as the proportion of haemorrhoidectomies that can be performed as day cases is much greater with the stapled technique.

Conclusion: The stapled haemorrhoidectomy is rapidly becoming established as an effective treatment of haemorrhoidal disease, and may soon become the procedure of choice. It enables most procedures to be performed as day cases.

Colorectal imaging

There has been increasing interest over recent years in the advent of imaging the colonic mucosa without the need for endoscopy using CT or MR colonography – so called 'virtual colonoscopy'. Both modalities are developing rapidly, and many centres are now publishing promising results. Pappalardo *et al* (38) report a series of 70 consecutive MR colonographic studies with a sensitivity of 96% for detection of endoluminal lesions, which equates to published data of colonoscopic detection rates. A series of 105 CT colonographic studies (39), had a sensitivity of 93% for the detection of polyps at least 1cm in size and 70% for polyps of 6 to 10mm.

Whilst their role in the assessment of known colonic disease is probably limited, improvements in both techniques may make them suitable in the future for colonic screening because of their non-interventional nature.

Preoperative staging of colorectal carcinoma is now an integral part of

Table 1. The Risk of Dukes A carcinoma or high grade dysplasia according to type of adenoma.

Morphology of Adenoma	Likelihood of Dukes A carcinoma or high-grade dysplasia (%)
Small Flat lesions	4
Small Polyps	6
Large Polyps	16
Large Flat lesions	29
Depressed lesions	75

management planning to help decide the optimal treatment for an individual patient, which may include neoadjuvant or adjuvant radio- or chemotherapy, as well as identifying those lesions suitable for local resection.

Endoanal ultrasound (EAUS) uses a 7-12 MHz anal probe to give circumferential ultrasound images of the rectal wall. This technique demonstrates the muscle layers well, and can predict tumour spread through the rectal wall. In the largest published series Mackay *et al* (40) report the results of a series of 433 patients in which the overall sensitivities for T-staging varied between 66% for T2 lesions to 89% for T4 lesions, whilst that for penetration to perirectal fat was 83% and lymph node involvement was 67%.

Those factors which determine prognosis from colorectal cancer i.e. tumour invasion, lymph node status and circumferential resection margin can now be accurately imaged by MRI scanning. MRI imaging of rectal tumours planned for resection is becoming routine practice to determine which patients should undergo preoperative radiotherapy. Brown *et al* (41) first published data in 1999 showing MRI staging and pathological correlation in 28 patients. In 2003 the same group published a study of 98 patients showing 94% agreement for T staging, 85% for nodal status and 92% for circumferential resection margin positivity (42). Larger multicentre studies are currently underway (MERCURY-2) to examine this issue.

Endorectal coil magnetic resonance imaging presents a further refinement whereby a magnetic coil is placed endorectally prior to scanning. Comparative studies in 26 patients by Gualdi *et al* (43) show better results than endoanal ultrasound, but not significantly so. They report an accuracy of 85% for T staging and 81% for N staging. The place of this technique may be in conjunction with EAUS when the results are equivocal.

Conclusion: Endoanal ultrasound is currently the optimal modality to assess early rectal lesions for resectability. MRI is the optimal technique for staging rectal cancers at present. CT and MR colonography are likely to become more commonplace as a screening procedure.

Alternatives to open surgery for colorectal carcinoma

Aside from laparoscopic surgery, there are two further new techniques in colorectal cancer treatment (transanal endoscopic microsurgery (TEMS) and endoluminal stenting) that are potential alternatives to open surgery in certain circumstances.

TEMS was developed for the transanal excision of large benign lesions which would have previously required anterior resection, and for treatment of early cancers in those patients who are considered unsuitable for major transabdominal surgery. The

technique was first described in 1983 and involves using a large operating endoscope inserted via the anus, and long instruments similar to those used for laparoscopic surgery; recurrence rates are generally around 10% for T1 lesions and 25% for T2 lesions (44). A recent single centre UK series of 102 TEMS from Leicester (45), reported a 6% recurrence rate for adenomas, but a 20% (3/16) incomplete resection rate for T1 and T2 tumours, although there have been no recurrences after later definitive surgery.

Endolumenal self-expanding metal stents are now available and can be placed across tumours of the colon and rectum as an alternative and possibly preferable way of managing patients presenting with malignant large bowel obstruction. The first reports of stenting using these devices were in the mid 1990s, but they have rapidly become part of the modern management of colorectal cancer. Stents can be successfully placed endoscopically, radiologically or by a combined approach (46). Initially their use was limited to palliation, but they are being increasingly employed as a bridge to elective resection in those patients who have potentially curable disease. In a recent review, Harris *et al* (47) suggested that 60-100% of obstructing colorectal cancers could potentially be amenable to successful stent placement, with good palliation in those patients who have unresectable tumours.

Khot *et al* have recently published a comprehensive systematic review of stent procedures for obstructing colorectal cancer (48) including data on 598 patients from 29 series. There was a remarkably low mortality of 0.5%, and an overall perforation rate of 4%. The rate of perforation after preliminary balloon dilatation however was 9.5% compared to 2.4% without dilatation; thus pre-dilatation of malignant strictures is to be avoided. Technical success was achieved in 92%, clinical success in 88% and migration of stents occurred in 10% after placement. Stenting was palliative in 56% and used as a bridge to elective surgery in 44%. Decompression was successful in 85%, allowing a single stage surgical procedure in 95% of stented patients. Successful stent placement allows recovery from obstruction, and time for pre-operative staging. Those patients found to have incurable disease are then left with the option of avoiding unnecessary major surgery and the possibility of a stoma with excellent palliation in most cases. Stent placement is cost effective, with a €2933 saving per stented patient overall, and €1140 for each patient proceeding to surgery (49).

Conclusion: TEM procedures are safe and appropriate for benign rectal lesions and for T1 tumours, but the place of TEM in T2 tumours is unclear at present. Stenting appears to be cost-effective, safe and effective with low mortality and morbidity, but further randomised controlled trial data is required.

Breast Surgery

Skin sparing mastectomy (SSM)

Although the mutilating radical mastectomy has largely been consigned to history, simple mastectomy still removes a large area of skin overlying the breast tissue. The consequence of this becomes apparent during reconstruction, when not only breast volume but skin need to be imported leaving an aesthetically poor donor site. The combination of small incisions with subcutaneous excision of the glandular tissue means an oncologically satisfactory mastectomy can be performed leaving the breast skin envelope behind. Coupled with immediate reconstruction, this facilitates reproduction of the correct size and shape of the reconstructed breast and minimises donor site morbidity. Whilst cosmesis is important in breast reconstruction, the most important factor is continued oncological safety and a series of reports have now outlined reasonably long-term results of SSM and immediate reconstruction. In a series of 176 operations with a median follow up of 73 months, Medina – Franco *et al* (50) report a local recurrence rate of 4.5%. Carlson *et al* report a 2.7% local recurrence rate in a series of 118 procedures at mean of 42 months follow up (51) and Rivadeneira (52) compared the local recurrence rate over an 8 year period between their SSM and non-SSM and found no difference. Most of these reports have been of patients with early breast cancer, but similarly impressive results have come from a series from Foster *et al* (53) who achieved a local recurrence rate of 4.5% at 49 months median follow up in a cohort of 25 patients with locally advanced (Stage IIB and III) breast cancer. Further attempts to reduce donor site morbidity have yielded the Envelope Mastectomy and Immediate Reconstruction (EMIR) procedure in which the SSM and latissimus dorsi muscle harvest both take place through a single linear mid axillary line incision (Figure 2) (54). There is no donor site scar.



(a)

Fig 2. (a) Results of a right EMIR procedure (anterior view). (b) The procedure is performed through the single lateral mammary fold incision and there is no donor site scar viewed from behind (c).



(b)



(c)

Conclusion: Skin sparing mastectomy is oncologically safe and can improve breast reconstruction. Single incision procedures are feasible and can further improve the overall cosmesis of mastectomy and breast reconstruction.

Endocrine therapy of breast cancer

Tamoxifen, a non-selective oestrogen receptor antagonist, has been the mainstay of adjuvant endocrine therapy for breast cancer for 30 years. It has been credited with achieving a 20-30% reduction in breast cancer mortality over that time span (55). A large randomised trial (ATAC) of a newer class of hormonal agent, Anastrozole (a 3rd generation aromatase inhibitor) demonstrated superior efficacy to tamoxifen in the adjuvant setting. Over 9000 post-menopausal women with hormone sensitive breast cancers were randomised to receive tamoxifen, anastrozole or both in combination and followed for 5 years. Anastrozole alone showed a statistically significant improvement in disease-free survival compared to the other two groups, as well as a significant reduction in the incidence of contralateral breast cancer. It also had a lower incidence of associated thromboembolic events (56). Anastrozole has also been shown to be superior to tamoxifen as 1st line therapy in postmenopausal women with advanced breast cancer (57) and better than

megestrol acetate as 2nd line therapy in advanced breast cancer that had progressed on tamoxifen (58). A further new agent, Fulvestrant, has also been licensed for the 2nd line treatment of women with cancers progressing under hormone therapy and has demonstrated equal efficacy to Anastrozole in this setting (59).

Conclusion: Although novel hormonal agents are now available with superior efficacy than the 'gold standard' of tamoxifen, it is the consensus opinion of the American Society of Clinical Oncology (60) that until the trial data has matured further, Tamoxifen should remain the 1st line adjuvant treatment for post-menopausal women with early breast cancer.

Immunotherapy for breast cancer

The discovery that 20-30% of breast cancers over-express the human epidermal growth factor receptor-2 protein (HER-2), an independent adverse prognostic factor, led to a search for new biological therapies. Trastuzumab, an anti-HER-2 monoclonal antibody, has been shown to confer benefit in HER-2 positive women with metastatic breast cancer. In clinical trials (61) in combination with chemotherapy it significantly increased time to disease progression and mean survival, and reduced the 1 year mortality rate compared to chemotherapy alone. Similarly, single agent Trastuzumab has been shown to be effective as 1st line therapy for metastatic breast cancer overexpressing HER-2 (62). An important reservation with these studies is that the greatest benefits accrue in patients who overexpress HER-2 the most; partial overexpression responds significantly less well (63), which has implications for who should receive this costly therapy.

Conclusion: Immunotherapy has a role to play in the treatment of certain well-selected patients with breast cancer. It should be given as early as possible in the course of the disease. It is expensive.

Chemotherapy for breast cancer

It is now over 25 years since improvements in disease free survival and overall mortality after adjuvant chemotherapy – cyclophosphamide, methotrexate and fluorouracil (CMF) – were first demonstrated. Assessing improvements in chemotherapy regimens is problematical – large trials are needed to detect small differences in outcomes and there is an almost limitless number of different drug and dosage combinations to be trialled. However, it is now becoming clear that advances have been made in chemotherapy schedules, with an anthracycline/cyclophosphamide regimen as current standard. Addition of a taxane (docetaxel or paclitaxel) has shown improved response rates over standard. Palmeri *et al* (64) described an overall

response rate to 1st line sequential doxorubicin – docetaxel of 73.5% in women with Stage III and IV breast cancer. In another study of 44 women with metastatic breast cancer (65), paclitaxel – doxorubicin achieved an overall response rate of 71% including a complete response in 13 patients. Mean overall survival time was 28.4 months. In comparative studies, taxane-containing treatments again show marked benefit. The response rate was significantly higher (68% v 55%) in a paclitaxel-doxorubicin regimen than for fluorouracil-doxorubicin-cyclophosphamide (66) coupled with lengthened time to progression and overall survival.

Another agent of current interest is Capecitabine, a fluorouracil prodrug that is preferentially activated at the tumour site. It acts synergistically with other agents such as docetaxel, with which it may be given as combination therapy after anthracycline failure, and is also active as monotherapy. Capecitabine-docetaxel was significantly more effective than docetaxel alone, with significantly increased response rates and median survival time as well as reducing risk of disease progression and death (67).

There are a myriad of ongoing Phase III trials seeking to elucidate optimal chemotherapy regimens, utilising combinations of anthracyclines, taxanes, fluorouracils and monoclonal antibody therapies.

Conclusion: Taxanes have improved the response rates of adjuvant chemotherapy and further improvements are likely with newer agents and combination therapies.

Sentinel node biopsy (SNB)

The most important prognostic factor in breast cancer is the presence or not of axillary nodal spread. To ascertain this, patients have traditionally undergone clearance of all accessible axillary nodes, which is both diagnostic and therapeutic. Axillary node clearance has a heavy associated morbidity with lymphoedema and reduced shoulder movements prominent. SNB has developed to obtain accurate axillary staging information without the associated morbidity of clearance. Peritumoural injection of a radioisotope and / or a vital blue dye can be detected in the first – or sentinel – node draining the tumour. If the sentinel node is involved, then appropriate therapeutic clearance of the axilla can be performed; if the sentinel node is not involved then the remaining axillary nodes are highly unlikely to be involved and can be safely left in situ. The proof of this particular pudding is in the long-term local recurrence rates, for example, does this technique leave behind involved nodes to propagate early local recurrence? Large multicentre studies such as the ALMANAC trial (68) are well underway but figures from single centre case series are impressive. Hansen *et al* (69)

report a series of 238 SNB-negative early breast cancer patients followed up for between 6 – 69 months (mean 39 months) with no cases of axillary recurrence. Similarly, Veronesi *et al* (70) report 280 cases of SNB-negative breast carcinoma. They found no axillary recurrences, compared to the 7 predicted from the 343 'years at risk' evaluated. It is accepted that there is a false negative rate associated with SNB, although its clinical impact has been described as "low" in a study from Australia (71). SNB followed by axillary clearance had a false negative rate of 7.9%, although the authors claimed suboptimal treatment would have been offered to only 0.7% of trial patients. This is half the 1.4% false negative rate for SNB (as witnessed by axillary recurrence) described by Chung *et al* (72).

Conclusion: Sentinel node biopsy is likely to become the method of choice for staging the axilla, replacing node clearance and subsequently reducing axillary morbidity. It is unlikely to become routine practice until ALMANAC and similar randomised trials have reported.

Upper Gastrointestinal Surgery Barrett's Oesophagus

Barrett's oesophagus refers to the glandular intestinal metaplasia that can occur within the normal squamous epithelium of the oesophagus, which is associated with an increased risk of developing oesophageal carcinoma. The reported incidence of oesophageal cancer in Barrett's oesophagus varies widely, but a risk of approximately 0.5% annually is a generally accepted rate and since survival after oesophageal cancer is stage-dependent, it is thought that survival may be enhanced by endoscopic surveillance. The presumed mechanism of development of Barrett's oesophagus is a dysplasia-carcinoma sequence whereby specialized columnar epithelium progresses through low-grade dysplasia, high-grade dysplasia, intramucosal carcinoma, and submucosal carcinoma; the time course for this progression is highly variable, and most patients do not actually progress. Moreover, since most patients with Barrett's oesophagus will not die from oesophageal cancer, and many are not fit for the oesophageal resection that a diagnosis of high grade dysplasia or carcinoma entails, the benefits of endoscopic surveillance are the subject of wide debate. A recent survey of gastroenterologists in the UK by Mandel *et al* (73) revealed a variable practice, with 76% feeling surveillance was worthwhile, but only 41% following the British Society of Gastroenterology guidelines by taking multiple biopsies. New mucosal ablation treatments such as laser, endoscopic mucosal resection, photodynamic therapy

and argon beam photocoagulation are contributing to the debate by allowing less interventional control of oesophageal dysplasia in Barrett's segments.

Argon beam photocoagulation (APC) is a diathermy technique where the current is carried to the tissue in a flow of argon gas causing surface ablation. Morris *et al* (74) report 55 cases of ablated Barrett's with a mean follow up of 3 years after APC, and no incidence of carcinoma, conversely Basu and colleagues (75) reported 50 cases with macroscopic clearance after argon beam therapy, but there were remaining buried metaplastic glands in 44%, and recurrent Barrett's in 68% of patients at one year follow up.

Endoscopic mucosal resection has been reported in a German series of 70 patients with high grade dysplasia and early carcinoma (76). They achieved a 3 year survival rate of 88%, offering a real alternative to oesophagectomy for early stage disease in those unfit for major resection.

Photodynamic therapy is a technique in which the patient is given a precursor drug that accumulates in the target tissue which is then subjected to a specific frequency laser light, activating the precursor to an active molecule which ablates the local tissue. This method has been reported by Ackroyd *et al* (77) to markedly reduce the area of Barrett's in a series of 18 patients, and this reduction is maintained at 2 years follow up.

The NdYAG laser has been used for tissue ablation for many years and has also been used in Barrett's oesophagus. Weston *et al* (78) reported 17 cases of high grade dysplasia and early cancer ablated with NdYAG with no recurrences at follow up.

Conclusion: Surveillance of Barrett's oesophagus has always been controversial as the treatment for detected high grade lesions has had an unacceptable morbidity and mortality profile for many patients and clinicians. These new, less invasive therapies may mean that surveillance is worthwhile and should be extended.

Robotic surgery

The very use of robots to help perform surgical procedures may have once seemed inconceivable, but robotic surgical assistance has now developed to the point where these devices are available and whilst robotic surgery is not a development specific to Upper GI surgery, this is where it has found many of its early applications. There are two basic systems in use; the first is a robotic assistant where instruments, usually a laparoscope or retractors, are controlled by a robot while the surgeon operates in the conventional manner; the second is tele-robotic surgery where the robot acts as the surgeon and the surgeon controls the operating robot from a control console in the operating room. The console

could theoretically be placed distant from the operating theatre, but to date, the time delay in the robot response to controls has been a significant problem when controlled more remotely. These robots offer operating positions for the surgeon that are ergonomically superior to those required by traditional laparoscopy. Speech recognition technology has also allowed devices in the operating theatre such as the table, lights and robotic assistants to be controlled by the surgeons voice during surgery. A combination of voice control and robotic assistance can be used to provide a responsive, accurate assistant in theatre.

A number of robotic devices are commercially available and the best-known are:

- da Vinci Surgical System.
- ZEUS Robotic Surgical System.
- AESOP Robotic System.
- HERMES.

The da Vinci and ZEUS are robotic operating systems, whereas AESOP and HERMES are robotic assistant and theatre control devices. The potential benefits lie in the precision of movement afforded by robotic surgeons; even the most dedicated surgeons have a degree of hand tremor whilst moving, whereas a mechanical arm will remain absolutely steady and this precision is maintained throughout the course of a long procedure without becoming fatigued. The da Vinci system has been programmed to compensate for tremors, so if the surgeon's hand does shake, the computer ignores it and keeps the mechanical arm steady. Both da Vinci and ZEUS use 3-D imaging to provide the surgeon with a three-dimensional video operating field.

Luketich *et al* (79) have recently reported results from a study where 30 cases were randomised to HERMES or traditional assistance. In the non-HERMES cases, assistants were interrupted to make adjustments an average of 15.3 times per case versus 0.33 times per case in the HERMES cases ($p < 0.01$). Satisfaction scores were higher for HERMES cases for both surgeon and nurses. Similarly Merola (80) reported a controlled trial of colectomy and found no difference in operative time, morbidity or length of stay using the AESOP system, but the surgeons felt the operation was easier, and one less person was required in theatre.

Because the da Vinci system was the first robotic operating system to obtain a permit to be used in the United States the majority of published literature relates to this system. Talamini *et al* (81) published a series of 70 upper gastrointestinal cases performed using the da Vinci system with a 17% conversion rate to either open surgery or conventional laparoscopy. The incidence of conversion and time taken to complete procedures seemed to decrease with

experience of the system. Giulianotti *et al* (82) have just published a large series of 193 patients with 207 thoracic, abdominal and vascular operations using da Vinci yielding a conversion rate of 3.6%, a morbidity of 9.6% and an overall mortality rate of 1.5%.

Conclusion: Robotic surgery offers potential solutions to some of the problems of traditional laparoscopic surgery, such as fatigue and camera shake, without increasing operating time or morbidity. Further advances in telecommunications technology will pave the way for entirely remote telesurgery.

Minimally Invasive Surgery

Upper gastrointestinal surgery is an area where minimally invasive techniques have come to the fore, after all cholecystectomy was the first laparoscopic procedure to gain general surgical acceptance.

Splenectomy: Laparoscopic splenectomy has become a widely accepted alternative to open splenectomy and in some centres is the technique of choice. The technical approaches have become standardised and reported by Corcione amongst others in their series of 105 cases (83). They found the technique easier than open splenectomy with minimal complications. Cordera *et al* (84) compared open and laparoscopic splenectomy, and found laparoscopic splenectomy to be significantly quicker, and associated with a shorter time to diet and discharge. For larger spleens necessitating removal for massive splenomegaly published data suggests that the hand-assisted technique of laparoscopic splenectomy is an easier alternative, which is no different in terms of operating time, hospital stay or complications from ordinary laparoscopic splenectomy (85).

Oesophagus: Oesophagectomy remains the mainstay of treatment for potentially curable oesophageal tumours, but is a major operation with considerable morbidity (around 70%) and mortality. In an attempt to reduce this morbidity some centres have developed less invasive endoscopic techniques to perform oesophagectomy. Initial results from Sutton (86) in a report of 10 thoracoscopic-assisted oesophagogastrectomies for lower third oesophagus tumours without thoracotomy, produced only one significant complication (an anastomotic leak successfully treated by stenting) and no deaths.

A further 18 cases of thoracoscopically-assisted oesophagectomies have been published in Japan (87) in which similar numbers of lymph nodes were harvested as compared to open surgery, implying adequate oncological clearance can be achieved endoscopically.

The laparoscope is also being employed in benign oesophageal disease with a report of 10 cases of achalasia treated laparo-

scopically by long oesophagomyotomy and fundopexy to prevent subsequent reflux; faster recovery with the same success rates were demonstrated in laparoscopic cases (88).

Anti-reflux surgery: Laparoscopic procedures are well established in anti-reflux surgery, although the degree of wrap of the fundoplication remains variable between different series. Most centres are now moving toward partial wrap procedures, since these have good results in terms of reducing reflux and a lower incidence of dysphagia. Watson *et al* (89) reported a series of 107 laparoscopic funduplications, 53 of the Nissen type and 54 an anterior fundoplication. At 6 months they found patients who had undergone anterior fundoplication experienced significantly less dysphagia for solid food and were more likely to be satisfied with the clinical outcome.

Bariatric surgery: Anti-obesity surgery can be successfully performed laparoscopically. Weiner *et al* (90) recently reported a series of 984 patients who underwent laparoscopic adjustable gastric band procedures. They describe no deaths or conversions to open surgery in their series, a band slippage rate of only 3.7% and a mean decrease in BMI from 47 to 32. Despite these excellent results many bariatric surgeons are returning to bypass surgery as the procedure of choice for weight reduction in the morbidly obese and Kreitz *et al* (91) have described 9 patients undergoing laparoscopic Roux-en-Y gastric bypass procedures. Although technically more challenging than gastric banding, they report conversion to open surgery in only one patient and a mean inpatient stay of just 1.2 days.

Pancreatitis: Whilst generally playing little part in the acute management of pancreatitis, surgery may be required for the complications of pancreatitis such as pseudocyst and ductal obstruction/distortion. For those pseudocysts that require intervention (over half), traditional treatment is by open cyst-gastrostomy or cyst-jejunostomy with all the attendant problems of laparotomy. In selected units this procedure is now being performed via the gastroscope and Beckingham *et al* (92) report a series of 34 pseudocysts deemed suitable for gastroscopic drainage. Drainage was achieved in 71%, with recurrences in only 3 of the 24 patients drained in this way. This technique has major advantages over open surgery since laparotomy is avoided, and when possible, recurrence rates are low.

Conclusions: Minimally invasive upper GI surgery continues to expand and improve and some of these techniques are becoming routine practice.

Advanced upper GI ultrasound

The development of high quality ultrasound probes that can be used via an endoscope or

laparoscope has led to considerable advances in upper GI sonography over the last decade. The endoscopic ultrasound (EUS) was initially used for staging oesophageal tumours, but has become more widely used for both upper gastrointestinal malignancy and choledocholithiasis. The use of the laparoscopic ultrasound has been most widely used in the pre-operative staging of tumours of the upper GI tract. Keinle *et al* (93) report a comparison of macroscopic assessment, endoscopic ultrasound and CT for the staging of oesophageal and cardia tumours in a series of 117 patients. They found that endosonography was the most accurate staging modality for overall preoperative staging of oesophageal and cardiac tumours and that only by this modality was the correlation between pre-operative staging and histology any better than chance alone. A series of 116 gastric tumours staged by endoscopic ultrasound reported an accuracy of 78% for T staging, 77% for N staging, and an overall sensitivity for resectability of 94% (94). Wakelin *et al* (95) compared CT scanning, laparoscopic ultrasound and EUS in the assessment of 36 patients with oesophago-gastric cancers. They found CT to be the best modality for locally advanced tumours, endoscopic ultrasound best for early tumours and locoregional nodal disease, and laparoscopic ultrasound the method of choice for distant metastases; they conclude sensibly, but not unsurprisingly, that the three techniques are complimentary. The current British Society of Gastroenterology guidelines (96) for the management of oesophageal and gastric cancer recommend that all tumours are staged spiral CT and endoscopic ultrasound.

EUS has also been shown to be useful for screening patients at risk of pancreatic neoplasms. In a small study, Gauger *et al* (97) showed that in 15 patients with multiple endocrine neoplasia syndrome who developed pancreatic tumours, endoscopic ultrasound detected the pancreatic neoplasms at an asymptomatic stage in 14 (93%).

In the treatment of choledocholithiasis EUS can be used for diagnosis of ductal stones, without the level of morbidity that accompanies ERCP. 485 patients with suspected ductal stones underwent endoscopic ultrasound followed by ERCP or surgery with assessment of the duct (98). This study identified 237 true positives, 2 false positives, 216 true negatives and 4 incomplete scans giving 98% sensitivity and 99% specificity. In addition, the investigators showed a cost benefit by not performing more invasive evaluation of clear ducts. De Ledingham *et al* (99) compared endoscopic ultrasound with magnetic resonance cholangiopancreatography (MRCP) in a

prospective controlled study of 43 patients and showed endoscopic ultrasound to have better results to MRCP, although the difference was not significant.

Conclusion: Endoscopic ultrasound is a quick, non-invasive, cost effective and accurate way of investigating upper gastrointestinal pathologies.

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