18th ANNUAL CONTROVERSIES AND PROBLEMS IN SURGERY

Venue: New Lecture Theatre. Faculty of Health Sciences
Date: 10 – 11 OCTOBER 2014
Theme: Recent Innovations and Difficulties in Surgery

Date Friday 10 October 2014
07h15 – 08h00 Registration

08h00-08h05	Introduction and Welcome	Prof Taole Mokoena
08h05-08h15	Opening Address by Deputy Dean	Prof Gerhard Lindeque
	Chairman: Dr Timothy Hardcastle	
08h15-08h35	Who should be captain of the ship (co-ordinator) in Polytrauma setting: i. Must be General Surgeon ii. Must be Orthopaedic Surgeon	 Dr Steve Moeng Prof Mthunzi Ngcelwane
08h35-08h55	How should Trauma Surgeons be Trained: i. General Surgeon's View ii. Orthopaedics View	 Dr Pradeep Navsaria Prof Mac Lukhele
08h55-09h15	Use of thoracoscopy in trauma	Dr Sorin Edu
09h15-09h35	Use of laparoscopy in trauma	Prof Zac Koto
09h35-10h00	Panel discussion with all presenters	All
10H00-10h30	**TEA AND VISIT EXHIBITIONS**	
		Chairman: Prof Thifili Luvhengo
10h30-11h00	Should ALL thyroid goitre be subjected to surgery: Yes No	 Prof René Botha Prof Taole Mokoena
11h00-11h20	Management of patient with axillary lymph node metastasis but occult primary	Dr Ines Buccimazza
11h20-11h40	What should be the criteria for adrenalectomy and what approach	Prof Zac Koto
11h40-12h00	Options for liver biopsy: percutaneous, laparoscopic, open	Dr Reshma Maharaj
12h00-12h20	Early recovery after surgery (ERAS)	Prof Thifili Luvhengo
12h20-12h40	Modern management of varicose veins	Prof Thanyani Mulaudzi
12h40-13h00	Panel discussion with all presenters	All
13h00-14h00	**LUNCH AND VISIT EXHIBITIONS**	
		Chairman: DR Elbashir Osman
14h00-14h20	Presentation and Management of Small Bowel Cancer	Dr Christian Jeske
14h20-14h35	Issues and challenges in Radiation treatment for Small Bowel Cancer	Dr L Mnguni
14h35-14h50	Issues on Medical Treatment of Small Bowel Cancer	Dr Jaqueline Kempen
14h50-15h00	Panel Discussion all presenters	All

15h00-15h30	**TEA AND VISIT EXHIBITIONS**	
		Chairman: Prof Otto Karusseit
15H30-16h00	Acute and Surgical Pain Management	Prof Christoffel Odendaal
16h00-16h20	Management of Chronic Nonspecific Pain	Dr Russell Raath
16h20-16h40	Chronic Pancreatitis Pain	Prof Martin Smith
16h40-17H00	Nerve blocks, spinal block and local anaesthetics	Dr Dwayne Möhr
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19h00-22h30	BANQUET	

Date **Saturday 11 October 2014**

07:30-08h00 Registration

		Chairmen: Dr Steve Moeng/ Dr Pradeep Navsaria
08h00-08h30	Fluid Therapy in Septic Patients: Crystalloids OR Colloids; Which, what product, when and how	Prof Jan Pretorius Dr Timothy Hardcastle
08h30-09h00	Principles of Damage Control in Trauma: i. Torso Trauma ii. Multiple Fractures iii. Neurosurgery iv. Vascular trauma	 Prof Meshack Ntlhe Dr Nkhodiseni Sikhauli Prof Sam Mokgokong Dr Chris Tsotetsi
09h00-09h20	Panel Discussion – Presenters	All
		Chairman: Prof Taole Mokoena
09h20-09h40	When is definitive surgery for peptic ulcer diathesis appropriate and what procedure	Prof Sandie Thomson
09h40-10h00	Pathology and management of Oesinophilic oesophagitis	Dr Fritz Potgieter
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10h00-11h00	**B R U N C H**	
		Chairman: Prof Sats Pillay
11h00-11h20	Management of Rectal Prolapse	Dr Hennie Pienaar
11h20-11h40	Management of incidental polyps during colonoscopy	Dr Mpho Kgomo
11h40-12h00	Panel Discussion – Presenters	All

		Chairman: Prof Meshack Ntlhe
12h00-13h00	Ethical Challenges in Palliative Surgery. When is palliative Surgery inappropriate OR Is palliative surgery always appropriate	Prof Gerhard Lindeque Prof David Cameron Dr Brendon Bebington Prof Magda Slabbert
13h00	VOTE OF THANKS	Prof Taole Mokoena

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Welcome Note

It gives me pleasure to once again welcome you to this our 18th Annual Controversies and Problems in Surgery Symposium 2014.

The Annual Symposium has become a feature in the Surgical Update and Continued Professional Development arena in South Africa and the Department is honored to present it.

We have chosen this year's theme as Recent Innovations and Difficulties in Surgery and trust you will not be disappointed.

There are a number of innovations being used in surgery. Some are driven by the industry while others are truly new ways of solving difficult problems. Surgery is often accompanied by difficulties both of the procedure itself but also of challenges of decisions on appropriate treatment for the individual patient. We hope that after this symposium we will reach a rational approach to the use of new technological advances and to decision making in many a difficult problem.

I should thank all the discussants for their preparatory work and their written submissions for the proceedings booklet. We know how busy you all are, thank you for taking time off for our symposium.

I wish to thank the Medical Industry for their continued support. Without your support we would not be able to host an affordable conference that is reachable by all surgeons especially our trainees. Please continue with your goodwill to the surgical fraternity.

Lastly I should like to thank all the staff in our Department. Your team work made the arrangement an easy and indeed enjoyable task.

Good luck.
Prof T Mokoena
Oct 2014

"WHO SHOULD BE CAPTAIN OF THE SHIP (CO-ORDINATOR) IN POLYTRAUMA SETTING: MUST BE GENERAL SURGEON": THE ULTIMATE TRAUMA SURGEON

MS Moeng

Introduction:

Trauma remains a pandemic in RSA with major annual cost to the economy. It affects predominantly young people with direct impact on their ability to earn a living. Severe head injury and major musculoskeletal injuries may result in severe disability. It may take as long as two years for a significantly injured polytrauma case to return to normal work. Unfortunately we still do not have a comprehensive National Trauma registry that allows us to evaluate the extent of the Trauma disease burden. The emphasis on mortality figures as a measure of this disease
nly delays definitive care and compromises patient outcomes. The presence of the emergency department does not guarantee excellent treatment of severely injureis only a tip of the iceberg.

Individual units continue to evaluate their quality of Trauma care, with major discrepancies in outcomes. Trauma systems remain fragmented in South Africa, and management remains poor in some centres. There are significant differences between trauma outcomes between rural and urban centres.

A good Trauma system should minimise time of injury to definitive care. This requires a well-co-ordinated Trauma system that sends an injured person to a nearest appropriate facility. Sending a severe head injury to a unit without a CT scanner, or even neurosurgical capabilities, od patients. Neither does admission to a private institution. Rehabilitation capabilities remain a challenge in state institutions.

Orthopaedic Surgical training is very intense, emphasising the art of orthopaedic repair. It offers craftsmanship that offers expert care of the muscle, tendon, joint as well spinal injuries and disease. Like other disciplines, it is complemented by allied medical workers for optimal outcome. Over the years, there have been great strides on what is achievable with current medical technology. However, there is little time spend on the primary care of systemically deranged cases; these are often referred to other healthcare givers.

General Specialist Surgical training on the other hand allows for more focus on system care that includes renal, respiratory as well as gastro-intestinal disease. This offers the General Surgical training an unfair advantage over Orthopaedic training to reinforce principles of holistic patient care and interpretation of common investigations. Typical patients seen during Trauma, Vascular, Hepato-biliary and Transplant rotations offer a backbone to the treatment of critically ill patients.

Overview and expectations for a Trauma leader:

Trauma leadership requires ongoing feedback to the whole system. This requires a dedicated person with special interest in Trauma who can constantly be responsible to improve the system within the cluster environment. An ongoing influence and impact on various pre-hospital transport modalities to improve standards as well as offer feedback mechanism aimed at ongoing education of pre-hospital personnel. Greatest challenge that we see is overloaded pre-hospital transport system as well as inappropriate triage on the field. These issues require a champion who can continue to put pressure for better care.

This responsibility for trauma education should not only be regional, but should be extended to both national and international scene. By ongoing structured Training the overall care will be uplifted. Institutions that are associated with universities should be able to offer internationally competitive training to both undergraduates as well as post graduates. The trick is in finding a practical solution to the local needs in our country. There is no debate that as South Africans we remain unique in our spectrum for Trauma as well exposure to penetrating Trauma than any other Trauma centres in the world.

The chain is as strong as the weakest link! Whatever training we offer, it should include all stake holders: paramedics, nurses, students, qualified personnel as well as specialist. That is why courses like ATLS®, DSTC™, NMTC™ are so successful. An appropriately trained medically trauma physician should be well vested in the basic sciences as well as the critical are concepts: something a generally trained surgeon is comfortable with compared to an orthopedically trained surgeon. This key background information allows for better development of Trauma protocols that offers a standard of care and optimize outcome. The protocol should cater for all possibilities, ranging from individual condition treatment, to approach of care on polytraumatized individuals.

Included in the community development should be a role to have outreach programs that are intended to inform the community. General participation in preventative measures will have a long term impact in reduction of Trauma. This measure goes hand-in hand with security cluster management of crime and disorderly behaviour. Dissemination of knowledge to the community via different media platforms can save a life. The aim is to influence the mind-set of the political powers to aid in developing appropriate systems to prevent trauma.

Constant evaluation of trauma services remains essential to success. Good quality mortality and mortality meetings should aim to have root analysis of outcomes and implement mechanisms to improve trauma care. These standards should maintain international norms and expectations. Active research participation should always be encouraged to allow for academic growth. Effective Trauma leader should encourage an environment that allows for ongoing growth of health workers and create a platform for teaching.

Major Trauma remains a systemic disease. Outcome of critically injured patients depend on severity of Trauma, the quality of care, the quality of Trauma system and the individual genetic component. There is very little room for error as patient tolerate multiple insults poorly. Ability to manage multiple systems as well as well as to support them adequately depends on excellent knowledge of the basic and advanced sciences. The abdomen is the most common site of missed injuries and this can be minimised by having a surgical input through-out the care of the patient. It is not sufficient to rely on radiological report for clinical judgement especially when in some centres only junior radiologists are available after hours.

<u>Specific expectations of a Trauma leader in an Emergency Department:</u>

Being in charge of the management of a polytrauma patients requires excellent leadership. The appropriately trained individual must make decisions that will benefit patient. To co-ordinate management of combined chest, head, abdominal, spinal and musculoskeletal injuries, in an injured patient requires skill. The more informed one is with injury patterns in these cavities the easier the interpretation and prioritization of relevant management. Well-structured academic Training centres offer this

background Training to General Specialist Surgeon; a critical advantage over Orthopaedic Training program. There was a time that Orthopaedic Surgeons spend a significant period during their training doing General Surgical training: these days a minimal exposure to qualify for Intermediaries is all that is required.

Unfortunately Trauma decision making is not only limited to individual injury patterns. Resource availability and constant triaging is required in our emergency departments. The definition of Mass casualty incidents includes what we commonly see in our casualty environments in the middle of the night on a typical Saturday evening. Multiple patients with urgent injuries will require a captain who is capable of triaging all these injuries and prioritizing care based on the physiology. Difficult decisions may include rationalizing ventilators or ICU to those with better outcomes. Yet be able to save many with less unanticipated deaths.

In other countries that see more Blunt Trauma, there is no debate that the most common operations are orthopaedic procedures. This has been worsened by non-operative strategies that are applied to haemodynamically normal patients with solid organ injuries. We still have a higher number of penetrating injuries requiring visceral surgical intervention in RSA. We still have resource limitations that can augment our non-operative strategies, like angio-embolization after hours, limiting our ability to manage some complex solid organ injuries without surgery. It remains critical to have a General Surgeon intimately involved in the management of these cases.

Early Trauma death is still related to severe head injuries as well as haemorrhagic shock. External bleeding and orthopaedic sites are easily detected in emergency departments. The concealed bleeding in the chest as well as the abdomen (including the retro peritoneum), are best monitored and managed by General surgeon. The ongoing supervision of the rescus by the General surgeon allows for ongoing detection of physiological changes involving these injuries. Ability to carry out procedures necessary to control visceral bleeding is an added bonus. It is imperative that they (Surgeons) take ownership of management of complex cases.

Clarke et al looked at errors involving referral from rural environment in RSA. In their study involving 1512 Trauma referrals, they had 142 errors noted. Assessment errors included the abdomen, chest and vascular injuries in most cases. The resuscitation errors included airway, chest and vascular access. This again demonstrates the need to have appropriately trained Surgeon in the management of Trauma cases. To be able to co-ordinate resuscitation effectively, you should be able to interpret the endpoints of resuscitation.

Damage control surgery and damage control resuscitation requires prompt assessment and execution. A Trauma leader should be able to select appropriate cases that will benefit from this approach. Overutilization of DCS should be avoided as this strategy of major Trauma care is associated with severe morbidity. The emphasis of care during this critical stage of exsanguination is not based on perfect bony alignment but urgent control of bleeding even in associated musculo-skeletal trauma cases. The current concepts of Goal Directed resuscitation as well as Goal Directed Transfusion required familiarity with physiological application and interpretation of Thrombo-Elasto-Gram (TEG) or even ROTERM.

Conclusion:

Trust is earned and not assumed. To be able to be a good leader and co-ordinate active resuscitation and joint care from other disciplines, you need to be comfortable with critical decision making. Surgical timing of even orthopaedic procedures must to

be co-ordinated with the physiology of the patient. It is clear to me that to optimize outcomes in major trauma and co-ordinate different teams is better suited for someone with General Surgical Training background, than Orthopaedic Training.

Trauma Training as a speciality has been approved in South Africa. The Training as a fellow after completion of basic specialization as a General Surgeon, allows for exposure to complex Trauma management as well as ICU care of these Trauma cases. It further allows for introduction to the Trauma system from prehospital, in-hospital to rehabilitation care, allowing for a grounded general Trauma knowledge. It further emphasis the need for outreach and research to constantly evaluate and improve Trauma care. It also improves knowledge of mass casualty management (Disaster management) in this unsafe world that we live in.

The time has come that major Trauma centres should be led by appropriately Trained Trauma Surgeons. Our Trauma populations deserve better. Ke nako!

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WHO SHOULD BE THE CAPTAIN OF THE SHIP IN POLY-TRAUMA SETTING

Prof M Ngcelwane, Dept. of Orthopaedics

The captain of the ship should be a surgeon, who in addition to the training in his / her speciality, is adequately trained in intensive care medicine, with good understanding of the body's physiological response to trauma.

The curriculum for training the surgical specialities in both general and orthopaedic surgery covers these aspects of emergency medicine. The difference lies on how much emphasis is placed by each of the two disciplines on the intensive care medicine part of their practice.

In orthopaedics the emphasis in the practice of the specialty has been on the advances in biomaterials and biomechanics, which form the bulk of the speciality both in academic teaching and in clinical practice.

Yes, orthopaedic surgeons can be in charge of the patient in poly-trauma, but they are generally not suitable for it. It will have to be an orthopaedic surgeon who has special interest in intensive care medicine, a rare species indeed.

The real answer to the question does not lie in the 2 surgical disciplines we are talking about here. The answer lies in the developing of a specialty of acute care surgeon.

This specialist should not only be trained in all aspects of intensive care medicine, but also should be trained in all surgical discipline/ procedures that need to be done in the acute stage to ensure survival of the patient. The acute care surgeon will be the answer to the question.

DAMAGE CONTROL SURGERY ORTHOPAEDIC PERSPECTIVE

Prof Mac Lukhele

Abstract
Multiple fractures represent one of the most common injury patterns in the emergency room. Optimal outcome requires team approach with oversight by trauma surgeon. Damage control surgery of torso takes priority over extremity as long as site of extremity bleeding is controlled.

Practical goals are to

1. Keep someone alive that would be dead without us
2. Prioritize treatment to prevent killing someone
3. Treat extremities injury to return to patient functional life

And all this is achieved by stopping the bleeding while resuscitating, minimize/control contamination and stabilize the extremities.

What is known
-benefit of resuscitation
-early long bone fixation is beneficial
-intramedullary nail (IMN) of long bones has systemic effect

We need clarity on
-If a vascular injury is diagnosed in the setting of associated orthopaedic injury, what is the operative sequence?
-How to predict bad consequence of IMN?
-When to convert external fixator to IMN?
- Optimal time of fracture repair in all patients?

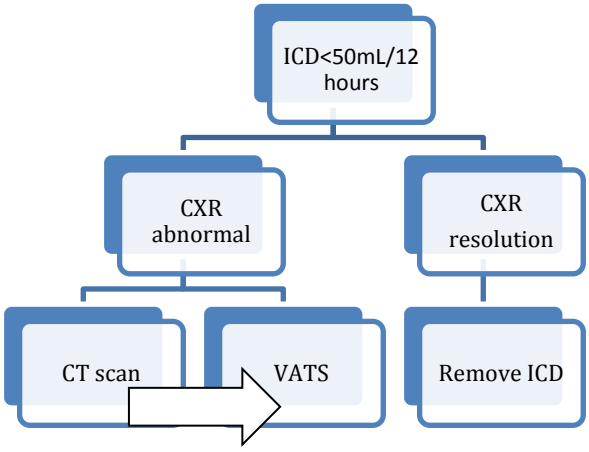
USE OF THORACOSCOPY (VATS) IN TRAUMA

Dr S Edu ,Trauma Centre, Groote Schuur Hospital

Video-assisted Thoracoscopy (VATS) is a well established technique in surgical practice. It's use in Trauma patients has been documented for more than 2 decades, particularly for retained hemothoraces, which constitute 5-10 % of trauma related hemothoraces.

The technique is quite straight forward and should be incorporated in an algorithm , clinical pathway, for the management of every retained hemotorax.
A review of the literature reveals that early use of VATS (< 5days), leads to less complications(empyema), smaller conversion rate to thoracotomy and a shorter hospital stay.

In this presentation we will describe the technique, propose an algorithm for the management of retained hemothoraces , discuss our centre's experience with VATS as well as the feasibility of VATS in a South African context.



ROLE OF LAPAROSCOPY IN TRAUMA

Prof Zac Koto, Medunsa

Introduction

The role of laparoscopy in trauma remains controversial at best although it may offer significant advantages to patients over the traditional open approach.

The evolution of laparoscopy in trauma

Laparoscopy has revolutionized all aspects of surgery and the last frontier to undergo significant change in minimal access surgery management is trauma.
Trauma surgeons have been very reluctant to embrace this strategy for a number of reasons.

Ivatury at al in 1993 published a report that showed small bowel injury missed rate of 80%. This was one of the first publications that raised a fire storm with regards to the usage of this modality in trauma patients.

Elliott et al in a prospective controlled study in 1998 reported missed injuries as high as 77%. The main concern was perceived unreliability in picking up small bowel injuries. Demetrius et al in evaluating 43 patients over a 4 year period, of these 18 had sustained blunt trauma and 25 sustained penetrating trauma. All of those patients underwent laparoscopy with conversion in 50% of blunt trauma patients and 36% of penetrating trauma patients. Overall laparoscopy was avoided in 58% of the patients.

The authors concluded that laparoscopy is safe for both blunt and penetrating injuries in carefully selected patients. It minimizes non therapeutic laparotomies. It allows minimal access surgery in selected patients with intra-abdominal injuries.

O'Malley et al in a systematic review using Pubmed database search found 51 studies of which only 13 were prospective. In most studies laparoscopy was used as a screening, diagnostic and therapeutic tool. 2569 patients underwent diagnostic laparoscopy for penetrating trauma, 1129 (43,95%) were positive for injury, 13,8% of those with injury had therapeutic laparoscopy. In total 33,8% were converted to open laparotomy, 16% of which were non-therapeutic and 11,5% of them were negative. 1497 patients were spared a non-therapeutic laparoscopy.

Overall 72 patients suffered complications. There were 3 mortalities and 83 missed injury. Sensitivity ranged from 66,7% - 100%. Specifically from 33,3% - 100%.

Conclusion of this review was that laparoscopy in penetrating injury may have an important role in selected subgroups of patients.
Surgeons' expertise is important. Laparoscopy has a screening, therapeutic and diagnostic role.

It is less reliable in detecting viscous injury. It has potential therapeutic and in centres that have the expertise.

Selection of patients

Using laparoscopy as a tool to selecting patients who should be converted to open laparotomy is well established and many units use it for this evaluation.

Occult diaphragm injury

Laparotomy has been very reliable in detecting and managing occult diaphragmatic hernia. Its role for this indication is less controversial and many units use it for this indication.

Laparoscopy for therapeutic purposes

A lot of debate has raged around the usage of laparoscopy for this indication. There is more data emerging that indicates the safety of laparoscopy for therapeutic purposes.

Our Institutional Policy

Our approach has always been to offer carefully selected patients (both penetrating and blunt trauma) who are hemodynamically stable laparoscopic approach with good outcomes over time.

The main caveat is the surgeons' expertise and this can be taught, even in a setting where these patients are offered laparoscopic assisted repair – patients still benefit

Conclusion

The role of laparoscopy in trauma is increasing.
There is no doubt that minimal access surgery will become the standard of care in carefully selected patients.

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IS THYROIDECTOMY THE OPTIMAL TREATMENT FOR GOITRE?

J.R. Botha. Wits Donald Gordon Medical Centre, Johannesburg

Introduction: The term Goitre refers to thyroid enlargement and is most probably derived from the Latin *guttur.*[1] The size of a normal thyroid is : <18 ml in females and <25 ml in males. These values pertain to individuals form iodine replete areas.[4] Enlarged thyroids maybe euthyroid, hyper- or hypothyroid, and maybe diffuse or nodular. Simple diffuse goitre(SDG) and or multinodular goitre(MNG) occur in areas of iodine-deficiency. SDG and or MNG can occur endemically (>5% of population affected) or sporadically (<5% of population affected). Toxic MNG is the commonest cause of thyrotoxicosis in iodine-deficient areas. More recently recognised is the Marine-Lenhart syndrome – this is a combination of Graves' disease and toxic multinodular goitre and is a rare cause of hyperthyroidism.[2,3] The risk factors of developing MNG is not clear, but it has been postulated that genetic as well as environmental factors are operative. Of the latter, iodine deficiency seems to be the most important risk factor.[4]

Knudsen, et al,[5] state: " ..thus, it follows that both endemic and sporadic goitre develop on the basis of genetic susceptibility interacting with environmental factors, and that the balance between nature (genetic factors) and nurture (environmental exposure) seems to correlate with the iodine intake. In areas of iodine deficiency the balance is towards nurture, whereas it is tipped towards nature in areas of iodine sufficiency." The study of Danish twins, by Hansen, et al.[6] further supports this concept, in that the monozygotic group had a higher concordance (0.57) as compared to the dizygotic group (0.36), for nodularity of the thyroid. In areas of iodine deficiency nodular goitre is common and in iodine sufficient areas goitre without nodules is more common.[4]

It is not clear whether SDG and MNG is the same disease, but at a different stage of development, and many studies do not differentiate between the two.[5] Tonacchera, et al [7] is of the opinion that in the early phase of goitrogenesis, goitres are diffuse and in time they become nodular. There is an increased incidence of thyrotoxicosis as well as malignancy(4%-17%) in MNG, and 50% of anaplastic thyroid carcinomas have a history of pre-existing MNG.

The genetic derangements in goiter are of interest, in that they are polygenic. No single gene being either necessary or sufficient by itself for disease development.[5] They are either thyroid-specific genes or thyroid-non- specific markers. In Familial goitre MNG-1 has been mapped on chromosome 14, MNG-2 on the X chromosome and MNG-3 on chromosome 3.[8] Other loci on chromosomes 2,3,7, and 8 have been identified in Danish, German and Slovakian families.[9] Well over a 100 naturally occurring and synthetic substances (goitrogens) have been reported to have effects on thyroid function or thyroid hormone metabolism.[10] The foetus and young children are at more risk than adults, especially in iodine deficient areas. There are (a) substances that inhibit iodine uptake (Perchlorate, Nitrate and Thiocynate), (b) compounds that inhibit thyroperoxidase (TPO) like Isoflavones, (c) compounds that decrease T_4 half-life, (d) compounds that displace T_4 from thyroid binding protein and (d) other substances that affect the thyroid.[10]

Treatment: The primary therapy of MNG or SDG, that are complicated by malignancy, is a total thyroidectomy.[11] There is lack of level I or II evidence available to favour either surgical or radio-iodine treatment in toxic MNG .[12] A total thyroidectomy will rapidly cure close to a 100% of these cases of their

hyperthyroidism, and will also cure the underlying multi-nodular disease, [13,14] relieve pressure symptoms, remove incidental foci of cancer and address the cosmetic problem of thyromegaly and will be more effective than radio-iodine. [12] On the other hand radio-active-iodine treatment is better than ultrasound-guided techniques of treatment, of toxic MNG.[15]

The nontoxic SDG that is small, with no history of radio-active exposure or familial history of cancer, can be watched. It has been my practice to advise them with respect of goitrogenic foods, smoking and iodine intake. In this group of patients, up to 20% in females and 5% of males, the goitre may stabilize or regress.[16] The indications to treat nontoxic SDG or MNG are: Pressure symptoms, cosmesis, retrosternal descend, discomfort and fear of malignancy. The modalities of treatment are: surgery, T_4 suppression, radio-iodine (with or without Recombinant TSH) and more recently ultrasound controlled percutaneous ethanol injection, laser therapy and radiofrequency ablation.[16]

Removal of all thyroid tissue (total thyroidectomy) offers the best chance of preventing recurrent MNG disease.[17] Conventional thyroid surgery is done through cervical incision, but currently the thyroid is being attacked trans-orally,[18] endoscopically through the axilla and breast,[19] in an endeavour to achieve no scar in the neck.

Although T_4 suppression therapy has previously been commonly used in goitre, its use now in thyroid nodules, is not recommended by the American Thyroid Association, in iodine sufficient areas. [20] A meta-analysis of six trials (609 patients) concluded that thyroid hormone suppression was more likely than placebo or no treatment to reduce nodule volume > 50%. However, long term treatment appeared to less effective, and regrowth was likely after cessation of thyroid hormone.[21] The disadvantages of this therapy is, low efficacy, poor compliance, the development of sub-clinical thyrotoxicosis, cardiovascular and bone disease and life-long therapy is required.

The use of radio-iodine therapy in non-toxic goitre is infrequent in USA and fairly common in Europe, in particular Denmark and Netherland. In most studies, the patients were elderly, had respiratory symptoms, dysphagia, or recent growth, and were considered poor surgical candidates or had refused surgery.[22] The median thyroid volume reduction was 40%-50%, within one year of therapy. In general radio-active iodine treatment of nontoxic MNG, is well tolerated, but 22%-58% became hypothyroid, 5% got transient hyperthyroidism and 3%-13% had symptomatic radiation thyroiditis. Furthermore 4%-5%, three to ten months later developed autoimmune thyroid disease (Graves' disease).[23] The life time risk of cancer following I^{131} treatment is 1.6%.[24] Pre-treatment with recombinant human TSH increases radio-iodine uptake by nontoxic multi-nodular goitres, and improves results.[25]

With the advent of ultrasound guided percutaneous ethanol injection and thermal ablation with laser or radiofrequency, thyroid nodules can be treated under local anaesthesia as outpatient procedures.[15] Although a 50% reduction in nodule size can be expected, these techniques unfortunately do not treat the underlying multi-nodular change which affects the whole thyroid gland.

S**ummary:** The treatment options of for this disease (SDG or MNG) are: observation, surgery, T_4 suppression, I^{131} with or without human recombinant therapy or percutaneous ultrasound controlled injection of alcohol, laser or radio-ablation of nodules. There are prospective trials comparing the other modalities of treatment to

surgery, which has been the gold standard. The choice of definitive treatment of nontoxic simple diffuse goitre and or multi-nodular goitre will depend on specific circumstances, surgical expertise, physician preferences and most importantly the preference of an informed patient.[26]

Once the decision to operate is made, a total thyroidectomy is the procedure of choice.[27] Care must be taken not to leave the pyramidal lobe behind, which may be on the left or right side, *bilateral* and sometimes not attached(9.4%) to the upper poles of thyroid gland.[28]

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SHOULD THYROID GOITRE ALWAYS BE MANAGED OPERATIVELY: IF SO WHAT OPERATION

Protagonist view by Professor Taole Mokoena

This presentation is going to argue for operative management of all thyroid goitres by operative means. It will further argue that total thyroidectomy is the only rational operative procedure.

Thyroid goitre is the most common endocrine abnormality. In the USA there are about 300,000 new cases per year. Goitre is more common in iodine deficient environments. The high thyroid goitre incidence in iodine deficient regions is associated with all causes of thyroid disorders including multinodular goitre, neoplastic disease and Graves' disease.[1, 2, 3]

Widespread use of radiological imaging for other diseases such as carotid vascular ultrasonography, cervical ultrasound for lymphadenophathy and CT scans uncover many asymptomatic and occult nodules within the thyroid gland.[4, 5] Such incidental thyroid nodules pose a management dilemma as many would remain asymptomatic.[6, 7] Autopsy after unrelated deaths also uncovered a high number of antemortem asymptomatic thyroid nodules.[8, 9]

A. Cancer in Nodular Benign Thyroid Goitre

The vexing problem is that a significant number of incidental thyroid nodules may in fact be malignant. Thyroid cancer that is treated at an early stage of its evolution carries a very good prognosis.[1, 2, 3] Therefore effort should be made to address these nodules early.

The problem then arises: which, if not all, incidental nodules should be treated actively. Thyroid ultrasonography (TUS) has been used to predict malignancy in thyroid nodules.[4, 5, 40] Fine needle aspiration cytology (FNAC) is currently the mainstay diagnostic modality for pre-operative diagnosis of thyroid malignancy.[39] FNAC is not infallible. A combination of TUS and FNAC especially ultrasound guided FNAC increases the diagnostic accuracy for malignancy but a significant proportion including the follicular thyroid carcinoma remains undiagnosed.[39] Follicular thyroid carcinoma requires histological diagnosis which can detect capsular vascular infiltration.[8, 9] Such histology is only possible after operative resection. Core needle biopsy (Tru-cut) is not suitable for this diagnosis.

I. Benign Non-Toxic Thyroid Goitre

Non-toxic thyroid goitre may harbour cancer. Table I shows that this problem is worldwide, both in iodine deficient and iodine replete regions. Cancer in a solitary nodular goitre (SNG) can be up to 17% while in multinodular goitre (MNG) it can reach 13%. In some regions up to 21% of nodular goitre can harbour cancer.

Table I. Incidence of Thyroid Cancer in Nodular and Toxic Thyroid Goitre

Reference	Country	Sample Size			Incidence %			Comment
		SNG*	MNG**	Combined	SNG	MNG	Combined	
McCall A et al 1986[10]	USA	96	69		17	13		Note men more
Smith JJ et al 2013[11]	USA			1523			15.6	Includes toxic MNG
Cole W 1991[12]	USA			663			8	Includes toxic SNG & MNG
Botrugno I et al 2011[13]	Italy			462			8.9	
Miccoli P et al 2006[14]	Italy			998			10.4	Includes toxic MNG
Cakir M et al 2007[15]	Turkey			375			6.9	Toxic Goitre
Cerci CC et al 2007[16]	Turkey			294			9.9	Includes toxic MNG
Anwar G et al 2012[17]	Pakistan			204			16.2	
Mermon W et al 2010[18]	Pakistan		105			7.6		
Abu-Eshy et al 1995[19]	Saudi Arabia			105			15.2	Includes lymphoma
Pang H-N et al 2007[20]	Singapore			268			21.2	
Koh KBH et al [21]	Malaysia		107			7.5		
Hanuma - thappa MB et al 2012[22]	India		100			10		
Bombil I et al 2014[23]	South Africa		107				3.7	Includes toxic MNG

* SNG = solitary nodular goitre. ** MNG = multinodular goitre.

II. Toxic Thyroid Goitre

i) Toxic SNG or MNG are commonly associated with benign adenoma or autonomous dominant nodule in MNG (Plummer's disease) respectively. While these are usually managed by low radio-active iodine ablation (RAIA) some may harbour malignancy which would otherwise be inadequately treated by such low dose RAIA.

ii) Graves' disease, including the paranodular variety may be associated with cancer.[11, 14, 15] Non-operative treatment may miss such cancers. Giving low RAIA for control of Graves' disease may not be adequate in such cases.

III. Cancer Following Radio-active Iodine Ablation Therapy

Radio-active iodine is widely used in both thyroid disease diagnosis and treatment. A number of cancers both within the thyroid gland and extrathyroidal have been described (Table II).

Table II. Cancer Incidence After Radioiodine Treatment

Reference	Country	Sample Size	Excess Relative Risk	Comment
Shore RE 1992[24]	USA	31000	up to 20 times	highest for high dose I^{131} among juveniles
Metso et al 2007[25]	Finland	2793	5/3 = 1.89	increased cancer in many extrathyroid sites
Hall P et al 1996[26]	Sweden	34104	up to 4.3	
Holm LE et al 1991[27]	Sweden	10552	1.3	increased cancer also in many extrathyroid sites
Hoffman DA et al 1982[28]	USA	1005	9.1	

B. Failure of Non-Operative Treatment of Thyroid Disease

I. Iodine supplement and L-Thyroxine (T4) suppression therapy for benign nontoxic goitre is gaining popularity. Only a minority (< 20%) of patients respond to iodine supplement alone. Less than 50% patients respond by reduction of the goitre on T4 treatment.[41] Furthermore when T4 treatment is stopped the goitre invariably relapses.[5] Lifelong T4 suppression is associated with significant side effects such as osteopaenia with its associated bone fragility, olopaecia and cardiac dysrhythmias and cardiac failure especially in older patients.[2]

II. RAIA therapy for Graves' disease is effective in up to 80%. About 20% of patients require repeat RAIA. Some patients may need even further RAIA sessions. It is in these failed RAIA patients that surgery should be resorted to.[29] Indeed we would argue that since the failure rate of RAIA is high and its success is invariably accompanied by hypothyroidism which requires lifelong T4 replacement, surgery should be offered as the primary therapeutic option.

III. RAIA is also being advocated for benign non-toxic MNG which require high dose [37] or recombinant human TSH augmentation for lower dose.[38]
Medical treatment of thyrotoxicosis and Graves' disease entails prolonged use of antithyroid drugs (ATDs), methimazole (carbimazole) or propylthiouracil, for a number of years. These are associated with side effects and complications including agranulocytosis and very rarely pancytopaenia which demand withdrawal in favour of alternate treatment such as surgery.[30, 31]

C. Treatment of Thyroid Goitre during Pregnancy

Definition of thyroid goitre during pregnancy includes disease after conception (or planned conception) and during the puerperium (6-12 months).
The challenge of managing thyroid goitre during this period is not only the wellbeing of the mother but also that of the foetus and the suckling neonate. Benign goitre treatment may be delayed until after delivery. However treatment of thyrotoxicosis and cancer may not.

I. RAIA is contra-indicated at any stage during pregnancy for its teratogenic effects during foetal organogenesis, intrauterine hypothyroidism and cretinism during foetal development, and neonatal hypothyroidism and growth retardation in the neonatal period as RAI crosses the placenta and is secreted in the milk.[1, 32]

II. ATDs treatment has teratogenic problems, particularly carbimazole (methimazole) which readily crosses the placenta more than propyluracil. Teratogenic effects are not only limited to thyroid dysgenesis but also includes abnormalities of the foregut such as choanal and oesophageal atresia.[33] The other side effects and complications already alluded would also extend to the foetus or neonate which receives the ATDs via the placenta or milk.

III. Surgical treatment of both cancer and thyrotoxicosis is the best option during pregnancy with a caveat that it be postponed until after the first trimester for fear of abortion and undertaken with precaution for good foetal preparation for maturity in the third trimester for fear of preterm birth.[32]

Which is the Best Operative Procedure for Thyroid Goitre?

This discourse excludes surgery for medullary carcinoma where there is general consensus that total thyroidectomy and lymph node dissection is the operation of choice. It also excludes anaplastic carcinoma in which surgery plays a limited role.

I. There is controversy around the use of total thyroidectomy versus lobectomy in SNG.

The protagonists for total thyroidectomy would argue that if the nodule turns out to malignant, completion (total) thyroidectomy is necessary but unnecessarily under a second anaesthesia for both papillary cancer which could be multifocal,[40] and for follicular cancer where RAI scan for detection of metastatic disease is necessary without normal functioning remnant thyroid tissue.

It is further argued that even when the index nodule is benign, there is still strong possibility of the presence or development of carcinoma (especially papillary) in the remnant lobe needing a second operation (Table I). Therefore total thyroidectomy should be done at the first sitting.

II. Controversy around the use of total versus subtotal thyroidectomy for MNG and Graves' Disease.

i) The principal argument for subtotal thyroidectomy for MNG is that it protects the recurrent laryngeal nerves (RLN) and parathyroid glands (PTG) from injury. However it leaves the patient vulnerable to recurrent MNG whose second operation is fraught with even more risk of RLN and PTG injury.
Proponents for total thyroidectomy would argue that RLN and PTG injury should be minimal in expert hands (less than 0.1% and 0.2% respectively).[34, 35]

ii) Protagonist of subtotal thyroidectomy for Graves' disease argue that this protects from RLN and PTG injury while leaving enough gland for production of physiological levels of T4 thus obviating lifelong T4 replacement therapy. Contrariwise, proponents of total thyroidectomy would argue that with subtotal thyroidectomy, it is not predictable that the remnant would not continue or relapse into producing (recurrent) toxic levels of T4. Furthermore the natural history of Graves' disease is that it burns out in 2-3 years requiring lifelong T4

replacement any way. Therefore T4 replacement is not eliminated but postponed by subtotal thyroidectomy.[36]

Summary

• It has been argued that although cancer of the thyroid is rare, it's early detection and surgical treatment is the mainstay of its management if cure is to be achieved.
• Nearly all apparently benign thyroid goitre both nodular and diffuse, toxic and nontoxic harbour a risk of occult cancer, up to 20% in some cases, which would automatically be addressed by primary surgical treatment.
• Many non-operative treatments for benign goitre have a significant failure rate which surgery does not carry.
• Increasingly RAIA is being preferred by some. In addition to its failure rate, it also carries a risk of cancer development both intra- and extra- thyroidal which surgery does not carry.
• ATD treatment for thyrotoxicosis is attended by risk of serious and life-threatening complications. Such patients are usually subjected to surgery.
• Surgery is the most safe treatment during pregnancy.
• Total thyroidectomy is the only operative procedure that accomplishes single step resolution of present and future problems of the thyroid. The inevitable life-long T4 replacement is a small price to pay for the peace of mind for both the patient and the doctor.

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MANAGEMENT OF A PATIENT WITH AN AXILLARY LYMPH NODE METASTASIS BUT OCCULT PRIMARY

Ines Buccimazza, Breast Unit, Department of Surgery, Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Durban

CONTENT

DEFINITION AND INCIDENCE

The occult primary or cancer of unknown primary site (CUP) is defined as the presence of metastatic cancer with an undetectable primary site at time of presentation. It is not a common clinical entity, accounting for 4% - 5% of all invasive cancers. [1]

The category of CUP represents tumours from many primary sites with varying biological behaviour. Patients are usually placed in one of four categories:

Adenocarcinomas	70%
Poorly differentiated neoplasms • Poorly differentiated carcinomas • Other o Poorly differentiated adenocarcinoma o Sarcoma o Melanoma o Lymphoma	20% - 25% 80% 20% 10% 10%
Squamous cell carcinoma	5%
Neuroendocrine carcinoma	1%

Adenocarcinomas comprise around 70% of CUPs. Squamous cell carcinoma comprises around 5% of CUPs, and is uncommon in the absence of an obvious primary tumour; the exception being patients presenting with a neck mass. Upper and mid-cervical lymphadenopathy is most frequently due to cancer in the head and neck region; inguinal lymphadenopathy have detectable primary sites in either the genital or anorectal area and adenopathy at sites other than cervical, supraclavicular or inguinal nodes usually represents metastasis from a primary lung cancer.

Less frequently, the lineage (carcinoma, lymphoma, sarcoma, melanoma, germ cell tumour) is unclear after light microscopic examination. These

histologic groups vary with respect to clinical characteristics, diagnostic approach, treatment and prognosis.

Patients with CUP typically present with symptoms referable to metastases. The clinical presentation is determined by the sites of metastatic tumour involvement, which may be multiple and often include the liver, lung, lymph nodes and bones. In autopsy series the most common primary sites are lung, pancreas, hepatobiliary tree and kidney, accounting for approximately 60% of cases. Other sites include the breast in women and prostate in men. The initial work-up, including physical examination, laboratory studies and imaging procedures often fails to identify the primary site in 20% - 30% of cases.

The prognosis for most patients with CUP is poor. Specialized immunohistological techniques that aid in tumour characterization have made the identification of specific sub-groups of treatable patients possible. A typical sub-group includes women (rarely men) who have adenocarcinoma or poorly-differentiated carcinoma in the axillary lymph nodes without an obvious primary breast lesion or distant disease after routine staging. Such patients are potentially curable when managed according to standard guidelines for stage II breast cancer.
This presentation will focus on axillary node metastases with an occult primary site.

DIFFERENTIAL DIAGNOSIS

Palpable axillary nodes are more often related to benign than malignant diseases. When a malignancy is identified, the most common tumour responsible for the axillary lymphadenopathy is breast cancer. The incidence of breast cancer resulting in metastatic axillary adenopathy in several series is ≥ 50%. Other neoplasms that may present with axillary nodal involvement are lymphomas, melanomas, sarcomas, thyroid cancers, skin cancers, lung cancers and less commonly uterine, ovarian, sweat gland or gastric cancers. The primary site is never identified in approximately 30% of cases of metastatic axillary adenopathy.

INITIAL DIAGNOSTIC WORKUP

BIOPSY

The first step in the diagnostic algorithm of a patient with unexplained axillary adenopathy is a biopsy, either a core biopsy or more commonly an excision biopsy. Standard light microscopic examination of hematoxylin and eosin-stained sections, immunohistochemistry and occasionally electron microscopy are used to narrow the differential diagnosis.

All adenocarcinomas share similar features: the identification of glandular structures formed by the neoplastic cells. Light microscopy cannot determine the site of the primary tumour. Certain tumour types have characteristic morphologic features eg. papillary features with ovarian cancer and signet

ring cells with gastric cancer; however they are generally not sufficiently specific to provide a definitive diagnosis.

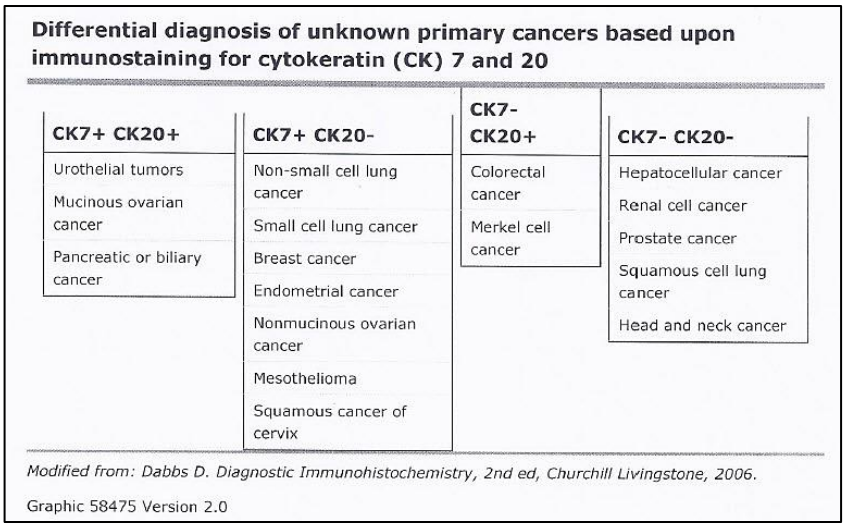
Immunohistochemistry (IHC):

If the biopsy specimen in a woman (or occasionally a man) with isolated axillary adenopathy reveals metastatic adenocarcinoma or poorly differentiated carcinoma, further immunohistochemical staining for specific markers should be undertaken. In some cases IHC may provide strong evidence regarding the primary site for some adenocarcinomas eg. positive staining for prostate-specific antigen (PSA) is quite specific for prostate cancer;

similarly the detection of thyroglobulin is relatively specific for thyroid cancer. In most cases IHC is not specific enough for definitive identification, but may suggest the most likely primary site. Thus, while none of the markers is sufficiently sensitive or specific to be used alone, patterns of expression may favour a specific diagnosis.

- Tumour markers: Carcino-embryonic antigen (CEA), CA 19-9, CA 15-3, CA-125 are generally not useful as either diagnostic or prognostic tests. Markers are often elevated in the serum of patients with adenocarcinoma of unknown primary site.
    - CEA: is a sensitive marker for adenocarcinomas of the breast, lung and gastrointestinal tract, but is unable to distinguish between these sites of origin
    - CA-125: is commonly positive in ovarian carcinomas, but is positive in around 10% of breast cancers. Thus its presence in an axillary node, particularly in conjunction with other compatible IHC findings, lends support to the diagnosis of an occult breast primary.
- Cytokeratins (CKs): the pattern of results with CK20 and CK7 may be helpful in suggesting a primary site
    - CK20 is normally expressed in gastrointestinal epithelium, urothelium and in Merkel cells
    - CK7 is expressed by tumours of the lung, ovary, endometrium and breast, but not in the lower GIT

      The presence of CK7 and absence of CK20 favours a diagnosis of breast cancer



- Estrogen receptor (ER) and progesterone receptor (PR): positive staining of an axillary lymph node supports a diagnosis of breast cancer particularly in conjunction with other compatible IHC findings. However, the markers are non-specific and may also be expressed in ovarian, uterine, lung, stomach, thyroid and hepatobiliary cancers
- Gross cystic disease fluid protein-15 (GCDFP) – identified by staining with monoclonal antibody BRST2. The latter is positive in 65% - 80% of cases and is relatively specific for breast cancer. Very rarely, it can also be positive in skin adnexal tumours, endometrial cancers and salivary gland tumours.
- Mammaglobin is more sensitive than GCDFP-15, but less specific for breast cancer. The two stains are typically used together. Mammoglobin stains positive for gynaecological, lung, urothelial, thyroid, colon and hepatobiliary tumours.
- Thyroid transcription factor (TTF-1): this is rarely positive in breast cancer, while it is positive in 70% - 80% of non-squamous lung cancers

HER2 staining is not generally useful in this setting as it lacks specificity. In addition, only 18% - 20% of breast cancers over-express the protein. Nevertheless, testing for HER2 over-expression by IHC or fluorescent in situ hybridization (FISH) is a routine component of the evaluation of all histologically proven breast cancers as it permits identification of patients who are likely to respond to treatments targeting HER2

Molecular tumour profiling (MTP):

Specific gene expression profiles are observed in cancers from different sites of origin. Molecular tumour profiling enables prediction of a tissue of tumour origin based on detection of site-specific gene expression profiles. Several molecular assays are commercially available using either RT-PCR or gene microarray techniques; however, these have not been directly compared with each other. Confirmation of the accuracy of MTP in predicting tissue of origin is difficult as the anatomic primary site rarely becomes manifest in these patients. The accuracy of MTP ranges from 75% - 85%. The role of MTP in the diagnostic evaluation of patients with CUP remains controversial. The National Comprehensive Cancer Network (NCCN) guidelines do not consider

gene signature profiling for tissue of origin to be a part of the standard management for the evaluation of an occult primary at present.

INITIAL CLINICAL EVALUATION

The initial evaluation should include a thorough history and physical examination, complete blood count, basic serum chemistries, urinalysis and computed tomography or magnetic resonance imaging of the chest, abdomen and pelvis, at a minimum. In men, the evaluation should include a prostate examination and measurement of PSA. In women, a pelvic examination and mammogram should be included.

Positron emission tomography computed tomography, although currently a standard diagnostic staging procedure in a large number of cancer types could only identify a primary site in approximately 40% of patients in a number of retrospective series.

Exhaustive imaging and endoscopic testing should not be performed as these studies rarely detect the primary site in the asymptomatic patient and confusion can result from false-positive results. It is recommended that specific signs or symptoms should guide the choice of additional studies.

BREAST EXAMINATION

Once the histological examination of the axillary lymph node biopsy specimen is completed and reveals an adenocarcinoma or poorly differentiated carcinoma, suggesting the breast as the primary organ, and breast cancer specific markers are found on IHC, the diagnostic work-up is targeted towards finding the breast primary. This consists of a complete physical examination of both breasts followed by breast imaging. Occult primary breast cancers constitute between 0.1% - 0.8% of all operable breast cancers. The incidence has not decreased despite improvements in breast imaging.

BREAST IMAGING

Mammography

A clinically occult lesion is identified on mammogram in only 10% - 20% of cases. Many occult lesions are missed because of their small size (in one series a ⅓ of occult breast primaries were ≤ 5mm in diameter) or because they are obscured by dense fibroglandular breast tissue.

Although mammogram may prove useful if it reveals a clinically occult lesion, not all abnormal mammogram findings indicate breast cancer. Suspicious findings warrant biopsy to confirm the clinical suspicion of an occult breast malignancy.

A negative mammogram in the appropriate clinical setting warrants further breast imaging evaluation with ultrasound and MRI.

Breast magnetic resonance imaging (MRI)

Breast MRI is more sensitive than either mammography or breast ultrasound for the detection of invasive breast cancers. Several small series have suggested that breast MRI can detect a primary breast cancer in approximately 75% of women who present axillary adenocarcinoma/ poorly

differentiated carcinoma and a negative clinical breast examination and mammogram. Breast MRI is now considered a standard approach to evaluate the breasts of patients suspected of harbouring an occult breast primary. The identification of a primary breast cancer by MRI may facilitate BCS instead of mastectomy.

The main draw-back of breast MRI is the high false positive rate (around 30% in one series) and difficulty localizing small contrast-enhancing foci. All suspicious findings on MRI require pathological confirmation. Some lesions identified on MRI can be located on subsequent targeted, “second-look” ultrasound and may then be amenable to biopsy under ultrasound-guidance.

For those not identified on ultrasound, targeting requires MRI-guidance. Hence, breast MRI should be performed with a dedicated breast coil by expert breast imaging radiologists at institutions where the capability to perform MRI-guided needle biopsy and/or wire localization of the findings is possible.
If a focal lesion is identified, further diagnostic evaluation should follow standard guidelines for suspected breast cancer.

MANAGEMENT OF PATIENTS WITH NORMAL IMAGING WORK-UP
In the absence of a palpable breast mass and normal imaging work-up of both breasts, the mammary origin of a metastatic adenocarcinoma/ poorly differentiated carcinoma to the axillary lymph nodes cannot be established with absolute certainty. However, if the histologic and IHC analysis is compatible, these patients are treated according to guidelines for stage II breast cancer.

COMPLETION OF STAGING WORK-UP
Exhaustive evaluation is not necessary. NCCN guidelines for the work-up of patients with isolated axillary metastases from adenocarcinoma or poorly differentiated carcinoma recommend only a chest and abdominal CT scan. Radionuclide bone scan is reserved for symptomatic patients or those with an elevated serum alkaline phosphatase. The use of PET-CT scanning is controversial.

LOCOREGIONAL TREATMENT

Axilla:
All patients should be subjected to a level II axillary lymph node dissection (ALND). This provides prognostic information that will guide further treatment and aids local control. Approximately 50% of these patients will have four or more positive lymph nodes which is an indication for post-mastectomy chestwall and supraclavicular radiation.

Breast:
The optimal treatment of the ipsilateral breast in women who do not have a discrete lesion is controversial. The options include mastectomy, breast conserving treatment using whole breast radiation therapy (RT) and observation alone i.e only ALND.

Mastectomy and ALND has similar outcomes to whole breast RT and ALND. [2]

Mastectomy: a standard approach is to perform a modified radical mastectomy at the time of axillary dissection. A breast malignancy will be found on histological assessment of the specimen in approximately 65% of patients. The primary tumour is usually < 2cm in diameter; in occasional patients only carcinoma in situ is identified. The benefits of local treatment were reported in a retrospective analysis of 51 cases of occult breast cancer. Women who had a mastectomy together with an ALND had a markedly lower rate of local recurrence compared to those who had no local therapy i.e ALND alone: 26% versus 77%. In addition disease-free and overall survival was also superior in the mastectomy group.

Radiation: the role of whole breast RT as a breast-conserving alternative to mastectomy in this setting is unclear. There is no level I evidence comparing this approach to mastectomy. The only available data is from small retrospective case series. In these published series, local control rates with primary whole breast RT range from 73% - 100%. In one of the largest non-randomised series that compared the two modalities, no significant difference was detected in locoregional recurrence (15% versus 13%), distant metastases (31% versus 22%) or 5 year survival (75% versus 79%) respectively in patients undergoing mastectomy and whole breast RT.[3]
However, in a later series of 53 patients with occult breast cancer, the 5 year rate of locoregional recurrence was lower in the RT group (28% versus 54%) and breast cancer specific survival was significantly higher (72% versus 58%)[4]

Observation: Published data on the local recurrence rate in the untreated ipsilateral breast with cases of occult breast cancer (ALND alone) have revealed that approximately 50% of women will develop an in-breast local recurrence.

Although some reports suggest that observation of the untreated breast does not adversely influence survival, some series suggest otherwise. A SEER database analysis from 1983 – 2006 identified 750 cases of occult breast cancer. Of the 470 patients who underwent ipsilateral breast treatment (mastectomy or breast-conserving RT), the 10-year overall survival was significantly higher than it was for the 126 patients who underwent ALND alone (65% versus 59%) or the 94 patients undergoing observation only with no surgery (48%). Mastectomy did not improve outcomes compared with breast conserving RT.[5]
Thus, in view of the high percentage of patients who will develop a clinically manifest tumour recurrence and the possible adverse effect on survival, observation of the breast without definitive local therapy is generally not recommended at most institutions.

ADJUVANT SYSTEMIC THERAPY

The benefit of adjuvant systemic therapy has not been systematically studied among women presenting with an axillary metastasis and an occult primary

breast cancer. At least one small retrospective report noted a significantly higher 5 year survival among the patients who received adjuvant chemotherapy as compared to those who did not – 93% versus 64%. [6]
It seems reasonable to extrapolate from modern treatment principles for clinically apparent breast cancer which includes adjuvant systemic therapy for patients with node-positive disease. Guidelines from the NCCN and others recommend chemotherapy for all women with node-positive breast cancer, irrespective of hormone receptor status. The addition of trastuzumab to adjuvant chemotherapy improves outcome in patients with HER2-overexpressing tumours. Adjuvant hormone therapy is recommended after the completion of chemotherapy for women with hormone-responsive tumours. [7]

POST-MASTECTOMY CHESTWALL RADIOTHERAPY

The addition of post-mastectomy radiotherapy in high-risk women reduces the risk of loco-regional recurrence, increases disease-free survival and reduces mortality from breast cancer.

PROGNOSIS

After treatment of an occult primary breast cancer with axillary metastases, the reported five-year survival rates range from 59% - 93%, with an average of around 75%. Some researchers suggest that the prognosis is better than that reported for stage II clinically apparent breast cancer.[8] This, however, is a controversial issue due to the small size of the series, marked heterogeneity in adjuvant treatment and the limited duration of follow-up in reports of patients treated for occult breast cancer. In the 2011 cancer statistics report from the American Cancer Society, covering breast cancer cases diagnosed between 1999 and 2006, the five-year survival among patients with clinically apparent primary tumours and nodal disease was 84%.[9] This compares favourably with that reported in the series of occult breast cancer.

METASTATIC DISEASE

Patients who present with metastatic axillary adenocarcinoma/ poorly differentiated carcinoma and no evident primary breast tumour, and who have metastatic sites in addition to the axillary lymph nodes should receive a trial of systemic therapy using guidelines for the treatment of metastatic breast cancer.

Patients with endocrine-responsive tumours may derive major palliative benefit from hormone therapy. Chemotherapy is indicated for patients with endocrine-unresponsive tumours as well as those who fail an initial trial of hormone therapy for endocrine-responsive tumours. Patients whose tumours over-express HER2 by IHC (3+) or FISH should be treated with trastuzumab in combination with other cytotoxic agents.

CONCLUSION [10]

Cancer of unknown primary site (metastatic axillary disease with an undetectable primary site at time of presentation) is not a common clinical

entity. Specific sub-groups of treatable patients have a favourable response to systemic therapy. Patients who present with axillary node metastases and an adenocarcinoma/ poorly differentiated histology, compatible IHC staining, no clinical breast cancer primary, negative breast imaging and no distant metastases present a potentially curable sub-set of individuals and are treated according to guidelines for stage II breast cancer.

These patients should all undergo a level II axillary dissection. Optimal treatment for the ipsilateral breast is controversial and ranges from a mastectomy at the time of ALND to whole breast RT after the ALND.

Observation alone of the ipsilateral breast is not recommended. In addition to the surgical management, these patients should undergo adjuvant systemic therapy according to published guidelines for stage II primary breast cancer; those subjected to a MRM may also require post-mastectomy chestwall RT. Patients with distant metastatic disease at presentation should receive treatment according to guidelines for metastatic breast cancer.

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WHICH CRITERIA AND METHOD IS APPROPRIATE FOR ADRENALECTOMY

Prof Zac Koto, Medunsa

Introduction

Laparoscopic adrenalectomy was first described by Gagner in 1992. Prior to this all adrenal pathology requiring surgery were addressed using open surgical techniques.

The advent of minimally invasive techniques changed all of these in the majority of patients. However there is still a subset of patients where open surgical approach is still preferred – these are patients with malignant tumours.

Criteria for adrenalectomy

Laparoscopic adrenalectomy is the standard procedure for hormonally active adrenal mass.

Patients with incidentalomas should be carefully evaluated for functional status and malignancy is still the major concern.

Tumour size of 6 cm or more for benign looking tumours should be considered for laparoscopic adrenalectomy.

The indications for adrenalectomy include the following:

- Adrenal hyperplasia
- Adrenal adenoma
- Adrenal carcinoma
- Isolated metastatic
- Incidentilomas

Choice of open versus laparoscopic surgery

The choice between these two approaches is open influenced by:

1. Body habitus of the patient
2. Specific characteristics of the tumour
3. Experience and skill level of the surgeon

What are the available open methods of adrenalectomy

1. The flank approach (posterior)
2. The transabdominal (anterior)
3. Trans-thoracic (thoraco-abdominal)

The posterior approach

The incision is made through the bed of the twelfth rib. One stays extra peritoneally to avoid accidentally entering both thoracic and abdominal cavity.
This approach seriously limits inspection of the peritoneal cavity. It is limited to smaller tumours (< 5cm) because of small incision. The down side of this approach is that for bilateral disease, two incisions are necessary.

The anterior approach

The incision is a long midline and this gives excellent exposure of the peritoneal cavity. Extra-adrenal disease can be addressed. Large tumours can be removed easily. Bilateral disease can be addressed simultaneously. However the morbidity is very high.

Trans-thoracic approach
The incision is midline and extended into the 10th and eleventh rib. The exposure is quite wide and gives excellent exposure. Larger tumours can be removed through this approach. The morbidity is high and limits abdominal exposure.

Minimal invasive techniques
Laparoscopy has now taken the centre stage for most adrenal pathology. The laparoscopic approaches available are:
1. Trans-abdominal (anterior)
2. Lateral trans-abdominal
3. Retro-peritoneal

Trans-abdominal approach (anterior)
The position of the patient is semi-lateral with the diseased organ up.
This approach has familiar landmarks but involves extensive dissection to expose the affected gland.

The posterior approach (retro-peritoneal)
The patient is placed in the jack-knife position.

A spacer is inserted to create working space below the 12th rib. The absence of landmarks makes this approach very challenging. The working space is usually small and therefor only small adrenal tumours can be removed using a retroperitoneal approach.

Lateral trans-peritoneal approach
The patient is placed in the lateral decubitus position and four trocars are inserted in the flank area.

This is the approach the author prefers. Large adrenal tumours can be removed using this approach.

Which method? Open or Laparoscopic
The only scenario where most investigators agree that open approach should be used is in the setting where malignancy is suspected.
If on imaging the following are encountered:
- Appears malignant
- Large tumours > 6 cm
- Proven malignant adrenal tumour

Advantages of laparoscopic approach
- Better cosmesis
- Low blood loss
- Decreased length of stay
- Early return to work

Laparoscopy should not change the indications for adrenalectomy

Conclusion
Laparoscopic adrenalectomy remains the best approach in carefully selected patients provided the surgeons has the expertise.
In the absence of the skills in minimal access surgery, open procedure is acceptable.

Ultimately the surgeons must choose the surgical method that they are comfortable with which will give the best outcome for the patient.
Malignancy of the adrenal should be approached by the open method preferably.

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OPTIONS FOR LIVER BIOPSIES: PERCUTANEOUS; LAPAROSCOPIC; OPEN

Dr Reshma Maharaj, University of Pretoria and Kalafong Hospital

INTRODUCTION:

The first liver biopsy was performed in 1883 in Germany by Erlich, a physician. The technique was modified by Menghini in the 1950's with the introduction of a "one second needle biopsy".

It became a gold standard in investigating liver pathology that had exhausted non-invasive clinical evaluation.

While this provided merely a descriptive report it represented the starting point for scoring systems and classifications relating to cirrhosis and fibrosis.

Unfortunately the liver biopsy is prone to a few pitfalls such as sampling error, intra- and inter-observer variability as well as pathologist experience; and is therefore actually an imperfect gold standard.

American Association for the Study of Liver Diseases (AASLD) liver biopsy recommendations

Focal disease and mass lesions

Liver biopsy should be considered in patients in whom diagnosis is in question, and when knowledge of a specific diagnosis is likely to alter the management plan.

Liver histology is an important adjunct in the management of patients with known liver disease, particularly in situations where (prognostic) information about fibrosis stage may guide subsequent treatment; the decision to perform liver biopsy in these situations should be closely tied to consideration of the risks and benefits of the procedure.

Technical issues, contraindications, and complications

Prior to performance of liver biopsy, patients should be educated about their liver disease and about investigations other than liver biopsy (if any) that may also provide diagnostic and prognostic information.

Prior to performance of liver biopsy, patients must be carefully informed about the procedure itself including alternatives (as above), risks, benefits, and limitations; written informed consent should be obtained.

Management of medications

Antiplatelet medications should be discontinued several to 10 days before liver biopsy, although there is uncertainty surrounding the need for their discontinuation. Management of specific compounds should be handled on a case-by-case basis, taking into account their clinical indications, as well as the potential bleeding risk associated with their use in the setting of liver biopsy.
Anticoagulant medications should be discontinued prior to liver biopsy. Warfarin should generally be discontinued at least five days prior to liver biopsy. Heparin and related products should be discontinued 12 to 24 hours prior to biopsy. In all patients,

the risk of discontinuing anticoagulant medications must be weighed against the (potential) risk of bleeding during/after liver biopsy.

Antiplatelet therapy may be restarted 48 to 72 hours after liver biopsy.

Warfarin may be restarted the day following liver biopsy.

Liver biopsy procedure:

Performance of liver biopsy requires an adequate sized and dedicated physical space suitable for focused physician effort as well as safe patient recovery.

The use of sedation, preferably light sedation, is safe and does not lead to increased procedural risk.

Vital signs must be frequently monitored (at least every 15 minutes for the first hour) after liver biopsy.

The recommended observation time after biopsy is between two to four hours and will vary depending on local expertise and practice.

Ultrasound guidance with marking of the optimal biopsy site performed immediately preceding biopsy, by the individual performing the biopsy, is preferred, though not mandatory, because it likely reduces the risk of complications from liver biopsy.

Contraindications:

Percutaneous liver biopsy with or without image guidance is appropriate only in cooperative patients, and this technique should not be utilized in uncooperative patients.

Uncooperative patients who require liver biopsy should undergo the procedure under general anesthesia or via the transvenous route.

In patients with clinically evident ascites requiring a liver biopsy, a transvenous approach is generally recommended, although percutaneous biopsy (after removal of ascites) or laparoscopic biopsy is acceptable alternatives.

Patients who require liver biopsy and who have a large vascular lesion identified on imaging should undergo the procedure using real-time image guidance.

The decision to perform liver biopsy in the setting of abnormal laboratory parameters of hemostasis should continue to be reached as the result of local practice(s) and consideration of the risks and benefits of liver biopsy because there is no specific PT-INR and/or platelet count cutoff at or above which potentially adverse bleeding can be reliably predicted.

Complications

Those performing liver biopsy must be cognizant of multiple potential complications (including death) that may occur after liver biopsy and discuss these appropriately with their patients beforehand.
Platelet transfusion should be considered when levels are less than 50,000 to 60,000/mL (this applies whether one is attempting biopsy percutaneously or transvenously).

The use of prophylactic or rescue strategies such as plasma, fibrinolysis inhibitors, or recombinant factors should be considered in specific situations, although their effectiveness remains to be established.

In patients with renal failure or on hemodialysis, desmopressin (DDAVP) may be considered, although its use appears to be unnecessary in patients on stable dialysis regimens.

Patients on chronic hemodialysis should be well dialyzed prior to liver biopsy, and heparin should be avoided if at all possible.

Radiological considerations:

Image-guided liver biopsy is recommended in certain clinical situations including in patients with known intrahepatic lesions (real-time imaging is strongly preferred) and in those with previous intra-abdominal surgery who may have adhesions. Image-guided liver biopsy should also be considered in the following situations: patients with small livers that are difficult to percuss, obese patients, and patients with clinically evident ascites.

Pathological considerations

Because diagnosis, grading, and staging of non-neoplastic, diffuse parenchymal liver disease is dependent on an adequate sized biopsy, a biopsy of at least 2 to 3 cm in length and 16-gauge in caliber is recommended.

It is recommended that if applicable, the presence of fewer than 11 complete portal tracts be noted in the pathology report, with recognition that diagnosis, grading, and staging may be incorrect due to an insufficient sample size.

If cirrhosis is suspected, a cutting rather than a suction needle is recommended.
In clinical practice, use of a simple (eg, Metavir or Batts-Ludwig) rather than complex (eg, Ishak) scoring system is recommended.

Noninvasive alternatives to liver biopsy

Liver biopsy is currently a fundamentally important tool in the management of patients with liver disease, important for diagnosis as well as staging of liver disease and its use is recommended until clearly superior methodologies are developed and validated.

Training for liver biopsy

Specific training for liver biopsy is essential and is recommended for those who perform it.

Liver biopsy should be taught to trainees by experts, highly experienced in the practice of liver biopsy and management of its potential complications.

Although the number of biopsies required to become adequately trained is unknown, it is recommended that operators perform at least 40 biopsies.
Training in percutaneous liver biopsy should include specific training in ultrasound interpretation of fundamental liver anatomy and other landmarks.

Image-guided liver biopsy should be taught to trainees by experts who themselves have adequate training and experience with the technique.

Data from: Rockey DC, Caldwell SH, Goodman ZD, et al. Liver biopsy. Hepatology 2009; 49:1017.

1. PERCUTANEOUS:

Percutaneous biopsies are the most commonly performed procedure with their limited invasivity, low rate of complications and brief post procedure monitoring.

It may be done either as a blind biopsy with the use of anatomical landmarks as a guide; or with the use of ultrasound marked ; or using real time ultrasound images for orientation of the needle.

The last option provides the lowest complication rate.

Recent studies have questioned the role of image guidance in parenchymal disease vs focal lesions – this being that guidance did not lead to a higher detection rate or a lower complication rate.

The advent of contrast enhanced ultrasound has also come to the fore especially in its role of biopsy of liver neoplasms – current studies evaluated the technical success rate of CEUS prior to biopsy as a means of increasing the detection rate.

Although widely used it is important to remember the complications that may arise as a result – bile peritonitis, haemobilia, bleeding, infection.

2. LAPAROSCOPIC :

Laparoscopic liver biopsy allows for adequate sample tissue under direct vision and allows for immediate haemostasis if necessary.

This technique is usually employed if abnormal liver lesions or disease has been identified prior to surgery.

The tissue may either be sampled by needle or a wedge resection.

An advantage of the technique is that it allows complete evaluation of the entire abdominal cavity especially with advanced disease.

TABLE 4. INDICATIONS FOR AND CONTRAINDICATIONS TO LAPAROSCOPIC LIVER BIOPSY.

Indications
Staging of cancer
Ascites of unclear cause
Peritoneal infections
Evaluation of an abdominal mass
Unexplained hepatosplenomegaly
Contraindications
Absolute
Severe cardiopulmonary failure
Intestinal obstruction
Bacterial peritonitis
Relative
Uncooperative patient
Severe coagulopathy
Morbid obesity
Large ventral hernia

Bravo AA et al N Engl J Med 2001; 344: 495-500

3. OPEN LIVER BIOPSY:

- This follows very much the same indications as laparoscopic.
- Most times the biopsy is either via needle or wedge resection if abnormalities are detected prior or at the time of surgery.

COMPLICATIONS OF LIVER BIOPSIES:

- Pain
- Intraperitoneal haemorrhage
- Intra- or extrahepatic haematoma
- Biliary – gallbladder perforation; haemobilia; bile peritonitis
- Pulmonary – pneumothorax; haemothorax
- Sepsis
- Seeding of a malignant lesion

ENHANCED RECOVERY AFTER SURGERY

Luvhengo TE
Department of Surgery, Charlotte Maxeke Johannesburg Academic Hospital/University of the Witwatersrand

Escalating health care cost which is already above 10% of some countries GDP. Key drivers of increasing cost of health care include laboratory and radiological investigations, technology driven service, aging population requiring operations and a litigant society. Major determinants of cost of care for surgical patients are consumables, length of hospital stay and time it takes for a patient to return to full activities including going back to work. Obviously the cost would increase dramatically if adverse event occurs during peri-operative care if a patient subsequently requires additional intervention such prolonged hospital stay, re-intervention and/or admission in ICU or high care unit.

Enhanced recovery after surgery (ERAS) is a coordinated and purposeful multimodal program to fast track recovery of patients after operation (Fearon, 2005; Murphy, 2007; Kehlet, 2008; Slim, 2011; Ypsilantis, 2009). The main aim of ERAS is to ensure that a patient recovers speedily and is able to go back to gainful employment as quickly as possible. It does not encourage bypassing of necessary steps in patient care but emphasize on expediting post-operative recovery taking short-cuts. Neither does ERAS encourage a health care worker to pick and choose which elements of the program to dramatize in his or her department/hospital (Fearon, 2005; Murphy, 2007).

Disliking use of nasogastric tube or insertion of surgical drains is not equivalent to practicing ERAS. Neither is preference of minimal access over open surgery early mobilization of patients or feeding within 24 hours. The ERAS program is a package comprising of a minimum number of steps (10-12 stretching to above 20 in certain in situations) purposeful incorporated into procedure specific patient care pathway. It is executed by a multidisciplinary team (MDT) made up of at least an anaesthesiologist, nurse, physiotherapist, dietician and a surgeon each of whom has a specific role to play throughout the process (Kehlet, 2008).

Essentials to ERAS program are elimination of harmful or unnecessary practices and adding what would augment recovery. It is divided into three phases: pre-operative, intra-operative and post-operative. And, in each phase all what each role player (member of MDT) has to ask is what to add and which practices to eliminate in order to dampen down intensity of post-operative systemic inflammatory response syndrome (SIRS) (Kehlet, 2008). For, there is a positive correlation between the magnitude of inflammatory response and severity of post-operative pain

Harmful pre-operative practices which ERAS program advises against are prolonged pre-operative stay, long fasting period, routine bowel preparation and sedation (Kehlet; 2008; Slim, 2011; Fearon, 2005). A patient should not meet an anaesthetist, dietician or physiotherapist for the first time in theatre or after an operation. Full outpatient work-up followed by same day procedure or admission just a day before or of the operation is advised. Long fasting period must be avoided and all patients must be allowed to eat whatever they like until six hours and drink high energy juice up to within 2 hours before surgery (Kehlet, 2008). Bowel preparation is a curse and; both under and under hydration (increase SIRS) must be avoided. Urine catheter in few occasions where it is needed must only be inserted only in theatre after a patient has been anaesthetised and be removed before he or she wakes up.

The following practices are encouraged: counselling (by all MDT members), appropriate antimicrobial and venous thrombo-embolism prophylaxis, evaluation by the same anaesthesiologist who is going to be involved during the operation (White, 2007) and if it not the case a responsible surgeon must refuse to continue. Strong motivation must be provided why the following where not given to a patient before transfer to theatre: anti-emetics, local anaesthetics, beta blockers, statins, insulin and glucocorticoids (Kehlet, 2008).

Adoption ERAS program does not interfere with practises proposed the WHO Surgical Safety Checklist. The following must be aggressively avoided: general anaesthesia, long acting anaesthetic drugs, nasogastric tube, urine catheter and long or vertical upper midline incision (Kehlet, 2008). Positioning of a patient for a procedure has to be appropriate (Philosophe, 2003). Transverse abdominal incisions are preferable where access would not be compromised. Minimal access surgery is advised only when it would significantly reduce the size of surgical incision, thus antecedent SIRS such for the following procedures: bariatric, anti-reflux, nephrectomy, etc (Kehlet, 2008). Additionally, fluid therapy is judicious (Rahbari, 2009) and hypothermia is avoided (Slim, 2011). Drains are used selectively.

Transfer a patient to ICU for post operative recovery only if it clinically indicated and attempts are made to extubate if it is possible. Surgeons only know how to hurt and therefore should not be allowed to prescribe analgesics. Multimodal post-operative pain management is followed with emphasis on a total ban of opioids to reduce the incidence of post-operative ileus (Kehlet, 2008) and urinary retention (Baldini, 2009). Nasogastric tube is must be removed immediately except after a difficult oesophagectomy and similarly urine catheter if it was not removed while a patient was in theatre. Only in exceptional cases should a patient still be NPO and receiving intravenous fluids 24 hours after a procedure (Fearon, 2005). Each patient has to be managed according to procedure specific care pathway with plans for each day including discharge day to aim for (Murphy, 2007).

Strict bed-rest is frowned upon and the same physiotherapist who evaluated and counselled the patient during the pre-operative phase would have seen him or her (the patient) and him or her to sit up within two hours and to start walking around soon thereafter. A dietician would do the same and feeding recommences within 24 hours except for patients who had upper gastrointestinal surgical procedures. Pharmacological treatment of ileus is only utilized if it is absolutely necessary (Slim, 2011).
The outcome of ERAS is early discharge not associated increase of morbidity and re-admission (not shifting cost centre) (Murphy, 2007). Reliable contact and access in the immediate post-operative period are ensured (Murphy, 2007).

The ERAS program is feasible in both developed and developing countries, and for various surgical procedures (Slim, 2011). Only hospitals practicing ERAS should receive NHI accreditation. The following operations should be done as Day Procedures and preferably under local anaesthesia: inguinal hernia repair, cholecystectomy, parathyroidectomy, thyroidectomy, etc. (Kehlet, 2008). Furthermore, patients who have had the following operations done on them should be discharged within 24 hours: bariatric surgery, anti-reflux surgery, prostatectomy, adrenalectomy, mastectomy,etc, (Kehlet, 2008).

As ERAS program has proven to be extremely successful a surgeon's licence has to be taken away or pay from his or her pocket if he or she keeps patients who have had the following operations for more than five days in hospital: open abdominal

aortic aneurysm repair (Murphy, 2007) oesophagectomy and pancreatectomy (Ypsilantis, 2009).

It is possible to implement ERAS anywhere and is urgently needed in resource-constrained countries. What is required is buy-in by key stakeholders and teamwork. Prior marketing, practicing and regularly reviews are advised (Kehlet, 2008). It works better where there has been metamorphosis of anaesthesiologists to become peri-operative care physicians (White, 2007), unless blood testosterone level in surgeons is dramatically reduced and health care practices are guided by reliance on a slightly better level of evidence than chronological age in practice. However, you will never enjoy the fruit of ERAS if as a surgeon you still shout at nurses and throw instruments on the floor.

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MODERN MANAGEMENT OF VARICOSE VEINS

Prof TV Mulaudzi

Varicose veins of the lower limbs are dilated, tortuous, and palpable veins that are typically larger than 3 mm[1, 2]. Varicosities are manifestations of chronic venous disease (CVD), which includes various other venous abnormalities, such as dilated intradermal veins, spider veins, reticular veins, and telangiectasia. Varicose veins are caused by either primary or secondary disease. According to Gloviczki et al.[3], primary venous disease, the most common cause of varicose veins, occurs as a result of an internal biochemical or morphologic abnormality of the vein wall. A prolonged period of standing is an important factor that leads to an intrinsic morphologic abnormality and progressive dilation of the superficial leg veins. Secondary causes of varicose veins include deep vein thrombosis (DVT), deep venous obstructions, superficial thrombophlebitis, congenital or acquired arterio-venous fistulas, and pressure on the veins in the abdomen during pregnancy or from a tumor[3].

Duplex ultrasound scanning is now the gold standard and first diagnostic test for assessing the lower limbs in patients with suspected varicose veins or CVD[3,6,7] .Duplex ultrasound scanning is a non-invasive, safe, reliable, and cost-effective test that can assess for venous obstructions, turbulence, and the direction of the flow of venous blood. It is important to evaluate the DVS for any obstructions, especially for those patients who have a history of DVTs, because an obstruction in the deep veins would affect any treatment of superficial varicose veins and would adversely influence long-term outcomes. The direction of venous blood flow is also assessed for any reflux. Retrograde, or backwards, flow that lasts for less than 0.5 seconds is normal (i.e., no reflux), whereas retrograde flow that lasts for more than 0.5 seconds is considered positive for reflux and would indicate the presence of incompetent valves or veins[7].

Varicose veins may be asymptomatic and may only be of cosmetic concern to some patients. However, treatment may be indicated for patients who are symptomatic. The management of varicose veins includes the use of conservative care, such as with lifestyle changes and compression therapy, and the use of more invasive treatments, such as surgery, endovenous thermal ablation, and sclerotherapy.

Conservative treatment for varicose veins includes various components. One first and very important step is to reassure the patient and to explain the mainly benign character of the disease. Serious advisory should be the first step and include life style changes such as weight loss, light to moderate physical activity and avoidance of factors that are known to make symptoms worse[8]. Compression therapy is the mainstay of active conservative treatment. It can cause the relief of symptoms of venous insufficiency[9]. However, there is no clear evidence that compression therapy can slow down venous disease progression or prevent recurrent varicose veins[10]. This may be due to the natural course of venous disease progression which is rather slow and challenging to investigate with high standard scientific trials. However, there is some evidence for the reduction of diurnal leg volume under compression therapy[11-13]. Therefore it may be supposed that progression of skin changes in patients with venous insufficiency can be prevented with a well advised and

compliant compression therapy. But compliance to permanent compression hosiery is rather remote.

The further role of compression therapy in the post interventional management of patients subject to various varicose vein ablation techniques is controversial and should be further investigated[14]. Another conservative treatment measure for chronic venous disease is the use of venoactive drugs. They are effective to some extend and may prevent symptoms, however, aetiological treatment of venous reflux and venous hypertension should be considered with priority.

Surgical techniques have been essentially modified after the introduction of anaesthesia since the middle of the 19th century. Today stripping and crossectomy such as avulsions of side branches is an accepted standard procedure. Various technical modifications have been introduced to avoid recurrence originating from the sapheno-femoral junction; however, none of them could be established as a standard measure.

Fisher et al. has followed up his patients after crossectomy and stripping of the great saphenous vein (GSV) for 34 years[15]. More than half of the operated patients had clinical recurrence of varicose veins, even more recurrence was detected by duplex sonography. In the light of these findings and the development of newer and less invasive treatment modalities surgery is nowadays challenged in its role as a golden standard treatment

The main downside of the surgical treatment is related to more postoperative pain and longer recovery time of the patient[16]. In the a recent document of the National Clinical Guidance Centre (NICE) surgical therapy is recommended in patients unsuitable for endothermal ablation by laser or radiofrequency or foam sclerotherapy to treat truncal varicose veins

Laser (light amplification by stimulate demission of radiation) was first described in 2001 for the treatment of varicose veins. Laser energy is converted in to heat inducing collagen shrinkage and fibrotic sealing of the vein lumen. Lengths of the waves, their delivery mode as continuous and pulsed, the radiation mode from the laser tip as radial and non-radial(tulip) and the material of the tip such as bare fibre or gold tip are technical characters influencing the impact of the destroying energy on both the treated vein and the surrounding tissue. This energy is defined per surface (J/cm) and should reach a certain level for effective varicose vein destruction. A minimum value of 60J/cm is suggested to achieve complete occlusion of the great saphenous vein without increasing the risk for complications.

The modality to treat varicose veins by endothermal radio- frequency ablation has been described by Goldman in 2000. The heat is generated by radiowaves, a type of electromagnetic radiation surrounding the active electrode. The produced electric current between these electrodes runs through the venous wall tissue generating heat. This heat is conducted to deeper tissue planes, causing collagen shrinkage, denudation of endothelium, and obliteration of the venous lumen.

Several studies have demonstrated that RF is equally effective as laser and surgery[17-20]. Post procedural pain after RF was suggested to be less intense when compared to EVLA 980 nm [20]. However, both techniques should be considered equally effective and safe.

Sclerotherapy can be performed as an outpatient procedure and involves injecting a chemical, either liquid or foamed, into the abnormal vein in order to destroy the

endothelium and induce fibrotic obstruction of the vein and may also be performed under ultrasonography[3]. Sclerosing agents used include sodium tetradecyl sulphate and polidocanol[6]. Complications reported from sclerotherapy are rare and include pigmentation, pain, and allergic reaction to the sclerosing agent, itching of the skin, thrombophlebitis, nerve damage, DVTs, and skin necrosis. However, several randomized trials have shown lower occlusion rates for primary truncal varicosity when compared to laser, radiofrequency or surgery.

Other minimal invasive treatment modalities for varicose veins were recently introduced; endothermal steam ablation, pharmaco- mechanical ablation (Clariveins) or the Venaseals device should be named. The two last mentioned techniques are performed without tumescent anaesthesia, another potential technical facilitation of the procedure that does not use heat and thus will not be associated with heat induced side effects. However, data are scarce so far and more high quality studies are required to show the potential role of these techniques in the future.

Endovenous therapy in the management of CVD has become an increasingly important means of restoring outflow of the venous system and providing relief of obstruction. Approximately 10% to 30% of patients with severe CVI can be found to have a significant abnormality in venous outflow involving iliac vein segments that contributes to the persistent symptoms.

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SMALL BOWEL CARCINOMA

Dr Christian Jeske, Department of Surgery, University of Pretoria and Steve Biko Academic Hospital

1. Epidemiology

1.1. Incidence

Despite the fact that the small bowel makes up 75% of the length of the digestive tract and 90% of its mucosal surface area, small bowel cancer is rare, accounting for less than 5% of gastrointestinal cancers.[1] The incidence of all small bowel cancers, according to the United States National Cancer Database, rose from 11.8 cases/million persons in 1973 to 22.7 cases/million persons in 2004.[2] The incidence of all malignant tumours of the small intestine ranges from 0.5 to 1.5/100000 in males and 0.2 to 1.0/100000 in females.[3] The incidence appears to be higher in North America and Western Europe than in Asia, with higher incidence rates in US black populations for both males and females.[2]

Adenocarcinoma of the small bowel (SBA) while infrequently encountered, accounts for 40% of all malignant small intestinal tumours. Most originate in the duodenum followed by the jejunum then ileum with about 10% having an unknown origin. The site and frequency of involved segments are as follows: duodenum 55-82%, followed by jejunum 11-25% and ileum 7-17%. [2,4-8] The increasing incidence is mainly due to the increase in duodenal tumours. The median age at diagnosis is in the sixth decade of life.

2. Etiopathogenetic factors

2.1. Environmental factors

In contrast to colorectal cancer, studies on the pathogenesis of SBA are constrained by the rarity of the disease. Alcohol consumption and smoking have been associated with an increased risk of SBA.[9,10] Other studies have reported an increased risk of SBA among highest consumers of sugar, refined carbohydrates, red meat or smoked food, while a reduced risk was observed with higher intakes of coffee, fish, fruit, and vegetables.[11,12]

The marked difference between the incidences of SBA and colorectal adenocarcinoma suggests different exposures to carcinogens. In the small bowel, the contact time between intestinal cells and xenobiotics or dietary carcinogens is shorter than in the colon, owing to the shorter transit time. In addition, the proximal small intestine contains low concentration of aerophilin Gram-positive bacteria. The density of the microbiota increases in the distal ileum, but is still much lower than in the colon, where the micorbiota produces xenobiotic transformation during which bile salts are deconjugated and dehydroxylated to form desoxycholic acid, which is a potential tumour promoter.[13] Moreover, the epithelial cells of the small bowel are equipped with a wide range of microsomal enzymes, including the benzopyrene hydroxylase, that may protect them against food-derived carcinogens.[14] There is however no clear explanation for the variability in incidence for the different sites where SBA can arise in the small intestine.

2.2. Carcinogenesis

The biology of SBA has been investigated only in a small number of patients. The main genes involved in colorectal carcinogenesis have been studied also in SBA (Table 1).

Table 1. Molecular changes in small bowel adenocarcinoma.

Reference	Number of patients	Abnormal p53	Abnormal ß-CATENIN	HER2 over-expression	APC mutation	KRAS mutation	dMMR phenotype
Wheeler et al.[15]	21	24%	48%	-	0%	-	5%
Arai et al.[16]	15	27%	-	-	8%	53%	-
Blaker et al.[17]	17	-	-	-	18%	-	12%
Aparicio et al.[18]	63	42%	20%	3.9%	-	43%	14%
Svrcek et al.[19]	27	52%	7.4%	-	-	-	7%
Overman et al.[20]	54	-	-	1.7%	-	-	35%
Blaker et al.[21]	21	-	24%	-	10%	57%	-
Planck et al.[22]	89	-	-	-	-	-	18%

The prevalence of the adenomatous polyposis coli (APC) gene mutation in SBA was reported to be rather low: 0/21, 1/15 (8%) and 3/17 (18%). [15,16,17] These data suggest that the carcinogenesis of SBA differs from colorectal carcinogenesis, because APC mutation is found in 80% of sporadic colorectal cancers. The APC gene mutation results in a loss of regulation of ß-CATENIN that accumulates in the nucleus. ß-CATENIN accumulation has also been found in SBA but rather as a result of gain-of-function mutation. Abnormal nuclear expression of ß-CATENIN was found in variable proportions of the cases analysed: 10/21 (48%), 12/16 (20%) and 10/20 (50%). [15,18,23]

Other abnormal protein expressions have been reported in SBA. Reduced membrane expression of E-CADHERIN was found in 8/21 (38%) cases of SBA.[15] Overexpression of the p53 protein was detected in nuclei of 5/21 (24%), 4/15 (27%), 26/62 (42%) and 14/27 (52%). [15,16,18,19] A loss of SMAD4 expression was found in 5/27 (18%) cases.[19] Furthermore, abnormal expression of the vascular endothelial growth factor-A (VEGF-A) and the epidermal growth factor receptor (EGFR) was found in 50/54 (92%) and 35/54 (66%) cases, suggesting that this type of cancer could benefit from treatment targeting these receptors.[20] HER2 expression has been assessed in two studies, showing only very limited expression, 1/54 (1.7%) and 2/51 (3.9%). [20,18]

Inactivation of the DNA mismatch repair (MMR) gene, which is found in around 15% of colorectal cancers, is variable found in SBA with frequencies ranging from 5-35% of cases.

These findings suggest that SBA and colorectal cancers share common carcinogenesis pathways. Nevertheless, the APC mutation is less often observed in SBA. The frequency of the MMR phenotype differs in SBA series but it is generally more frequent than in colorectal cancer, this could possibly be explained by an over-representation of Lynch syndrome as a result of selection bias in this cohort. Only a large study based on an unselected cohort will allow for the assessment of the frequencies of the various biological alterations involved in SBA carcinogenesis.

2.3. Genetic predisposition

2.3.1. Familial adenomatous polyposis (FAP)
FAP is a consequence of a germinal mutation of the APC gene. SBA is the second most common primary cancer location followed by colorectal cancer. Most patients with FAP (50-90%) have duodenal adenomatosis with 3-5% developing duodenal cancer.[24] Even though the risk of duodenal adenocarcinoma in a FAP patient is relatively low, it was the main cause of cancer-related death in patients following a coloproctectomy.

2.3.2. Lynch syndrome
Lynch syndrome is caused by a germ line mutation of a DNA mismatch repair gene, which exposes the patient to various types of neoplasia. Despite various levels of increased risk for SBA have been reported, the lifetime cumulative risk remains low: 0.6% and 1% according to Finnish and French registries respectively.[25,26]

2.3.3. Peutz-Jeghers syndrome
This autosomal dominant disorder resulting from the STK11 suppressor gene mutation, which predisposes to hamartomatous gastrointestinal tract polyposis. The adenocarcinoma originates from the intra-epithelial neoplasia observed in the hamartomatous lesions. A relative risk of 520 (95% CI, 220-1306) for SBA was observed in these patients.[27]

2.4. Other predisposing conditions

2.4.1. Crohn's disease
Crohn's disease induces chronic inflammation in every segment of the digestive tract. The chronic inflammation releases cytokines that interact with cell surface receptors and target genes that can promote carcinogenesis.[13] A relative risk of 33 (95% CI: 15.9-60.9) was reported in a 2006 meta-analysis.[28] Male gender, fistulating disease, early age at diagnosis, distal jejunal or ileal disease and extended duration of disease are associated with increased risk.[29] The SBA arises in an inflamed small bowel segment. In contrast to sporadic SBA, in Crohn's disease, this cancer appears in younger patients (fourth decade of life), and mainly in the ileal segment. The cumulative risk is estimated to be 0.2% after 10 years of Crohn's disease and 2.2% after 25 years.[30]

2.4.2. Coeliac disease
Coeliac disease is characterized by a lymphocytic infiltrate that induces immunological disruption and damage to the epithelial cells that can include premalignant changes, and could increase the risk of both SBA and small bowel lymphoma. In a Swedish registry study, the relative risk of SBA in patients with coeliac disease versus the general population was estimated to be 10.[31]

3. Diagnosis

3.1. Clinical presentation
The clinical features of small bowel adenocarcinoma may include one or more of the following: pain, obstruction, bleeding, anorexia, weight loss, perforation or in the case of a duodenal primary, jaundice. In a single-institution study of 491 patients, the most common principal symptom at diagnosis was abdominal pain (43%), followed by nausea and vomiting (16%), fatigue and anemia (15%), upper or lower gastrointestinal tract bleeding (7%), and jaundice (6%).[32] The variable nature of the

presenting symptoms combined with the lack of physical findings, can contribute to a delay in diagnosis in many cases. In one study, failure to obtain a proper diagnostic test or misinterpretation of test results accounted for delays of 8 and 12 months, respectively; by comparison, the estimated diagnostic delay due to the patient's failure to report symptoms was less than two months.[33] Because of the vagueness and non-specificity of the presenting symptoms, a high index of suspicion is essential for early diagnosis and treatment.

3.2. Diagnosis

In a single-center study of 217 patients with SBA diagnoses were obtained by upper gastrointestinal endoscopy (28%), surgery (26%), small bowel barium transit (22%), CT scan (18%), ultrasound (3%) and physical examination alone (3%). The diagnosis was mainly obtained at advanced stages, when 35% of patients had synchronous metastases and 39% had tumours with lymph-node invasion.[4]

For SBA, small bowel barium transit has a sensitivity of about 50%,[34] and CT scan have an overall accuracy of 47%.[35,36] It should be pointed out that in a context of obscure bleeding after upper and lower endoscopy, a small bowel investigation should systematically be done. New investigation tools, such as CT enteroclysis, MR enteroclysis, capsule endoscopy, and enteroscopy now allow for an extensive exploration of small bowel and should thus make early diagnosis possible. CT enteroclysis has a sensitivity of 85-95% for the diagnosis of small bowel tumour, and a specificity of 90-96%.[34,37]

Capsule endoscopy allows carrying out a complete small bowel exploration as an outpatient procedure, however it should not be performed in a context of sub-occlusion. When it is performed to explore obscure bleeding, the sensitivity for diagnosing a small bowel tumour is between 88.9% and 95% and its specificity 75-95%. [38,39] Double balloon enteroscopy can be used for a wide range of small bowel investigations. Nevertheless, this procedure is less convenient than capsule endoscopy, and should be used only if a biopsy or preoperative tattoo is required.

3.3. Other recommended investigations after SBA diagnosis

A thoraco-abdomino-pelvic CT scan to assess distant metastases, and an upper and lower gastrointestinal endoscopy to look for other tumours suggesting a predisposing genetic disease is recommended. A baseline plasmatic carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19.9 assay should be done, especially in advanced cases, because the levels of these markers are of prognostic value.

In the context of a predisposing genetic disease or Crohn's disease, a full small bowel exploration should be performed to detect synchronous tumours. An assay of anti-transglutaminase A antibodies and a duodenal biopsy are recommended to detect coeliac disease.

Two different tests can be used to detect Lynch syndrome: the first identifies microsatellite instability by testing 5 microsatellite loci, and the second confirms the lack of expression of 1 or 2 mismatch repair proteins by means of immunohistochemical techniques.

4. Prognosis

SBA carries a poor prognosis at all stages, with a 5-year overall survival (OS) rate ranging from 14% to 33%.[2,4,5,8] The 5-year OS is correlated to the tumour stage. (Tables 2 and 3)

Table 2. Survival according to cancer stage and location.[4,6,7,8,40,41]

AJCC Stage	Incidence (%)	5-year OS (%)
1	4-12	50-60
2	14-30	39-55
3	19-27	10-40
4	32-46	3-5

SBA prognosis appears to be intermediate between those of colon and gastric cancers, and surgery for complete resection (R0) remains the only potentially curative treatment.[40] According to the NADEGE cohort, a locally advanced cancer found at surgery to be irresectable occurred in 5% of the cases.[6]

Lymph-node invasion is the main prognostic factor for local SBA.[4,40] The number of lymph nodes assessed and the number of positive nodes are of prognostic value. The 5-year disease-free survival rate was 57% if 1-2 lymph nodes were invaded, versus 37% if 3/> lymph nodes were invaded.[42] A lymph node yield of 10 or more was associated with a non-significant OS rate increase in stage 1 (73.2% vs 55.6%, NS) and a significant OS rate increase in stage II (61.8% vs 32.9%, $p<0.001$). Multivariate analysis identified advanced age, advanced stage, ileal location, the recovery of <10 lymph nodes, and the number of positive nodes as significant predictors of poor OS.[43] Therefore, curative resections at an early stage should include a regional lymphadenectomy.

One study reported 12/74 (16%) second cancers after a curative resection.[44] It is due to this high frequency of second cancers that justifies a prolonged follow-up after SBA treatment.

A retrospective study of patients metastatic or locally-advanced SBA treated with chemotherapy found that impaired WHO performance status and an above-normal value of CEA or CA 19.9 were prognostic for poor survival.

Table 3. TNM staging system for small bowel cancer.

Primary tumor (T)			
TX	**Primary tumor cannot be assessed**		
T0	**No evidence of primary tumor**		
Tis	**Carcinoma in situ**		
T1a	**Tumor invades lamina propria**		
T1b	**Tumor invades submucosa***		
T2	**Tumor invades muscularis propria**		
T3	**Tumor invades through the muscularis propria into the subserosa or into the nonperitonealized perimuscular tissue (mesentery or retroperitoneum) with extension 2 cm or less***		
T4	**Tumor perforates the visceral peritoneum or directly invades other organs or structures (includes other loops of small intestine, mesentery, or retroperitoneum more than 2 cm, and abdominal wall by way of serosa; for the duodenum only, invasion of pancreas or bile duct)**		
Regional lymph nodes (N)			
NX	**Regional lymph nodes cannot be assessed**		
N0	**No regional lymph node metastasis**		
N1	**Metastasis in 1-3 regional lymph nodes**		
N2	**Metastasis in four or more regional lymph nodes**		
Distant metastasis (M)			
M0	**No distant metastasis**		
M1	**Distant metastasis**		
Anatomic stage/prognostic groups			
Stage 0	**Tis**	**N0**	**M0**
Stage I	**T1**	**N0**	**M0**
	T2	**N0**	**M0**
Stage IIA	**T3**	**N0**	**M0**
Stage IIB	**T4**	**N0**	**M0**
Stage IIIA	**Any T**	**N1**	**M0**
Stage IIIB	**Any T**	**N2**	**M0**
Stage IV	**Any T**	**Any N**	**M1**

5. Treatment

5.1. Localised cancer

Complete resection (R0) of the primary tumour with locoregional lymph node resection is mandatory. In the context of posterior invasion, pre-operative treatment should be considered, and resection reconsidered after 2-3 months of chemotherapy.

Primary tumour resection in the presence of unresectable metastases is not recommended except in an emergency such as bowel obstruction, perforation or

uncontrolled bleeding. There is insufficient data to evaluate the value of metastatectomy in SBA.

For duodenal tumours, a Whipple resection with peri-duodenal, peri-pancreatic and hepatic lymph node resection and resection of the right side of the coeliac and superior mesenteric arteries needs to be performed.[4] An R0 resection is preferred, as R1 or R2 resections are strongly associated with poor prognosis.[46]

For jejunal and ileal tumours, an R0 resection with lymph node resection and jejuno-jejunal or ileo-ileal anastomosis should be performed. In case the last ileal loop or ileo-cecal valve is involved, a right hemicolectomy with ligation of the ileocolic artery, for adequate lymph node resection, should be performed.

To date no standard adjuvant regimen has been defined due to lack of randomized controlled trials. The only data available are those from retrospective studies. In a retrospective review of 48 duodenal adenocarcinomas resected with curative intent, chemoradiotherapy did not improve survival.[47] The data available do not establish a clear recommendation for radiotherapy in R1 or R2 resection or locally-advanced duodenal cancer. Several retrospective studies have found no benefit in adjuvant chemotherapy after potentially curative surgical resections of SBA. Despite the lack of evidence supporting the delivery of adjuvant chemotherapy for SBA, an analysis in the USA of the National Cancer Database has shown an increase in the use of chemotherapy from 8% in 1985 to 24% in 2005.[2]

5.2. Metastatic SBA

Very few studies have been published on the type of chemotherapy used for advanced SBA. Most of the studies available are small, retrospective or involve old chemotherapy regimens. Overall, they report a median OS of 8-18 months and objective response rates (ORR) ranging from 5% to 37%.[48-53] Several retrospective studies suggest that chemotherapy prolongs OS in patients with advanced SBA, but there is no agreed frontline regimen owing to the lack of randomized trials. A retrospective comparison of OS, according to whether palliative chemotherapy was prescribed, showed a significant increase of survival in treated patients (12 months vs 2 months, p=0.02).[4]

So far, no data is available for targeted therapy. The oxaliplatin-based chemotherapy seems to be the best choice.

For now, extrapolation of therapeutic interventions from other tumor types, such as colon and gastric cancer, are guiding therapy. Metastatic or locally-advanced small bowel adenocarcinoma has a poorer prognosis than colorectal carcinoma, but a better prognosis than gastric or pancreatic cancer with a median OS exceeding 12 months with chemotherapy.

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THE SMALL BOWEL AND RADIATION, CHALLENGES,

Dr Lindiwe Mnguni.
Supervisor: Dr K Lohlun

Radiation therapy is not regularly indicated in the treatment of small bowel disease.

Reasons are complex and related to the relative sensitivity of the small bowel to radiation, its mobility and the difficulty in defining the treated area.

We discuss Radiation induced small bowel disease – pathophysiology, clinical presentation, prevention strategies, and treatment.

There might be interesting future applications in this area.

ACUTE AND SURGICAL PAIN MANAGEMENT
Prof Lomby Odendaal

Definition of pain is as follows:
"Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is always subjective" IASP (International Association for the Study of Pain, 1986)

The classification of pain:

i. Acute Pain - will subside within reasonable time, (90 days) with or without treatment
ii. Chronic pain - lasts longer than six months, with or without treatment
iii. Cancer pain - combination of above mentioned

Another classification is

i. Nociceptive pain
ii. Neuropathic pain

I will spend time on discussing post-operative surgical pain
The best way to always treat pain is to stick the WHO ladder of pain treatment. 4 steps. Start with the first step which consist of basic analgesics e.g. paracetamol. The use of IV paracetamol, has become very popular in recent years. It is easy to administer.

If not effective, or even as an adjunct, add the second step which consist of NSAID,s. The most potent of these drugs still remains diclofenac but has the highest incidence of side-effects. Other very popular NSAID's are ibuprofen or indomethacin. The more advanced groups of these medications are the COX 2 anti-inflammatories, although not proven extremely effective, The combination of paracetamol and NSAID's is quite effective,

The mainstay of acute pain management still remains the use of opioids. Concerns still exist about the potential harmful effects on the patient – special reference respiratory depression.

Macintyre et al maintain the respiratory depression is only part of the problem and that the whole issue should be named "***Opioid induced ventilatory impairment***" – OIVI. This then include respiratory depression, decreased level of consciousness and upper airway obstruction.

Opioids given as treatment of acute pain should be carefully tritated and also very carefully monitored.

TOWARD BETTER UNDERSTANDING AND MMANGEMENT OF CHRONIC PAIN

Dr Russell Raath (MBChB MMed FIPP) Jakaranda Pain Clinic, Jakaranda Hospital Pretoria

The concept that **"pain is pain"** and that chronic pain is simply acute pain continuing for too long is simplistic, archaic and wrong
This misconception leads to:

1. General misunderstanding of what chronic pain is, which leads to

2. Inadequate and inappropriate treatment of the pain
    a. incorrect medication –
    b. medication dose escalation leading to -
    c. overdosing of medication
    c. unnecessary (repeated) special investigations (radiology - cost!!)
    d. unnecessary surgery or repeat surgery – especially spine surgery

3. General neglect of these patients:
    a. doctor doesn't know what to do anymore
    b. patients get told it's in their head – sent to psychologist or psychiatrist
    c. patients get told they must "learn to live with it"
    d. patients get told to 'change their behaviour'.

Traditionally, pain has been seen as a symptom of another underlying process or pathology which should go away once the underlying process or pathology has been eliminated and resolved. This fits in with the definition of Acute Pain and has a protective function

But sometimes the pain is chronic - by official definition if it persists for longer than 3 months. This 'time definition' of chronic pain is also is arbitrary and archaic.

a. Sometimes chronic pain is present and evident before 3 months have passed

b. Sometimes the mechanism for chronic pain is present form the outset – in other words the mechanism is chronic pain right from the start.

c. Sometime the **chronic** pain happens "on its own" with no apparent causative factor

Chronic pain is **NOT:**

a. simply a symptom of another underlying condition

b. "protective" like acute pain. It DOES NOT serve as warning of underlying condition

Chronic pain **IS:**

a. A medical entity, clinical condition and pathology in its own right

b. Destructive, serving no purpose at all.

There are different types of pain and booth types can be either acute OR chronic.

a. **Nociceptive pain** - pain “with a cause” - an inflammatory or non-inflammatory response to a noxious stimulus Nociceptive pain can be subdivided into

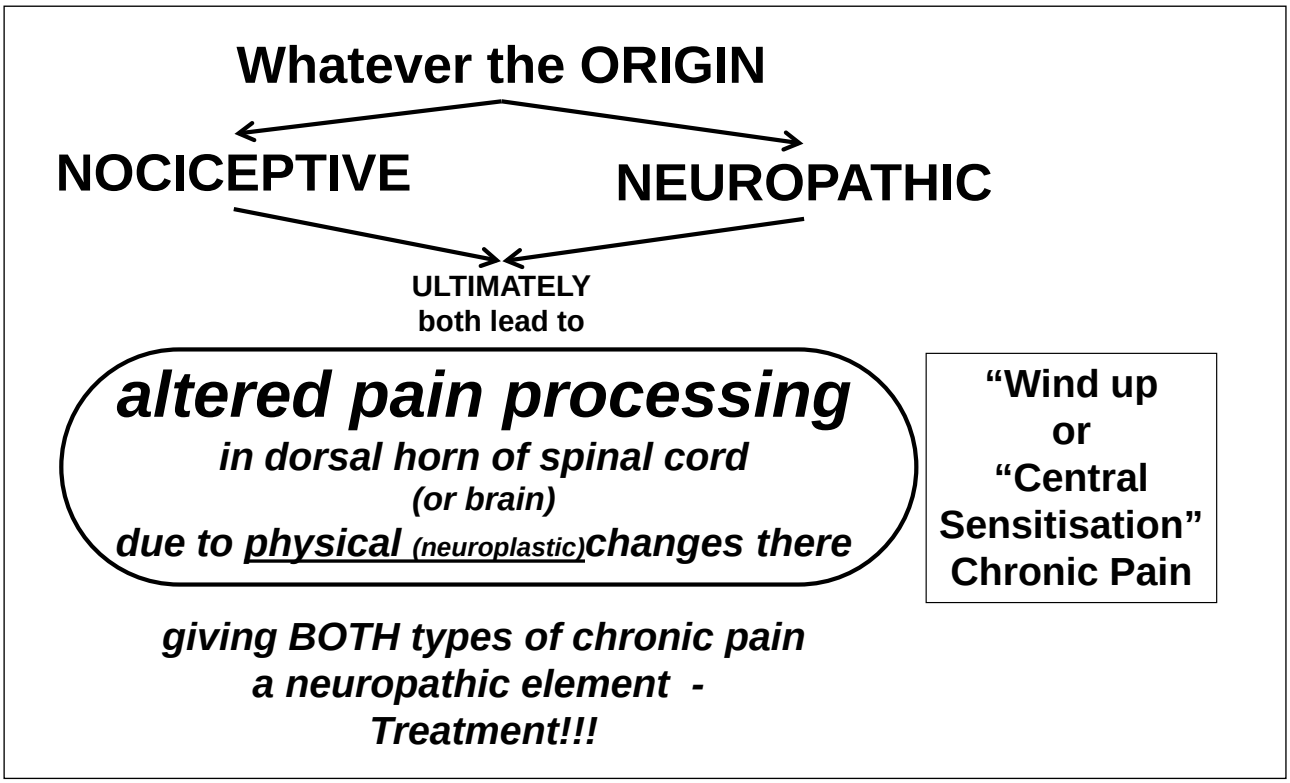
    1. **Somatic pain**

    2. **Visceral**

    as they are mediated by completely different nerve system and have their own characteristic.

b. **Neuropathic pain** - pain “without obvious cause” – initiated by a primary lesion (injury or spontaneous) or dysfunction in the peripheral or central nervous system - “Sick Nerves”

c. **Mixed pain** with nociceptive and neuropathic components



This altered pain processing and neuroplastic changes in the dorsal horn of the spinal cord is what constitutes “chronic pain”.

This presentation deals with how these neuroplastic changes and altered pain processing in the dorsal horn are mediated and possible better treatment modalities for chronic pain. As chronic pain and acute pain are not the same condition the treatment and management of each differs, sometimes markedly.

SURGERY FOR CHRONIC PANCREATITIS

MD Smith, University of Witwatersrand

There is a lack of consensus regarding the best treatment for chronic pancreatitis (CP). The condition usually presents with pain and as very little can be done to change the natural history of the disease process, our efforts are directed at improving the quality of life of the patients. A nihilistic approach to this condition based on evidence suggesting that the process burns out after 10 years is difficult to accept when one witnesses the suffering of these patients. Apart from pain, which is the most common presenting problem, there are other organ based complications of CP; strictures of the common bile duct, pseudocysts, vascular occlusions and hollow organ obstruction, that require a more aggressive approach due to their potentially life threatening nature.

Patients are often only seen by the surgeon many years after the onset of pain. The pain is often diagnosed as peptic ulcer disease (PUD) and treated as such, with the multiple recurrences treated again as PUD. These delays can be as long as 5 years. As health professionals we often do not take a detailed occupational history and as such past exposure to injurious domestic (wood burning fires and primus stoves) and occupational (petrochemical, printing and many others) exposures are not documented and appreciated. There is a strong relationship between CP and alcohol abuse. This is often aggravated by the co-existing depression that affects these patients. The substance abuse related to alcohol is often swapped for opiates further compounding the problem.

It can be difficult to judge the timing of surgery for pain. The nature of the other complications usually determines the timing of any intervention. Complete abstinence is not required before surgery is offered. There is some evidence that in patients who still consume alcohol in moderate amounts, the outcomes after surgery are better. As this operation is primarily aimed at quality of life improvement, it is very important that one does not rush into surgery as a solution. However having said that there is also evidence that earlier surgery before the introduction of opiates has better results for pain relief. There is also some evidence that suggests that earlier surgery does prevent progressive loss of exocrine and endocrine function. My approach is to counsel patients earlier on in the clinical process and then over a period of follow up the timing of surgery becomes obvious.

The aims of treatment of CP includes: pain relief, control of local complications, preservation of function, social and occupational rehabilitation, improved quality of life and exclude malignancy. The understanding of the pathophysiology of pain is still largely theoretical although exciting developments in this regard are emerging. Ductal hypertension, parenchymal hypertension, neo-proliferation of abnormal neurons and disordered spinal pathways are all proposed in isolation or various combinations as the cause of pain in chronic pancreatitis. This would explain why operations such as the Peustow lateral pancreatico-jejunostomy, which deals with one aspect only, have a fairly high failure rate. The head of the pancreas is regarded as the pacemaker for the pain, based largely on the fact that the majority of the mass of the pancreas is situated in the head. There is immunological evidence that the disease in the head of the pancreas may drive the inflammation process.

A host of minimally invasive neuronal ablation techniques have been reported. However concern for this approach in benign disease is based on the observation that recurrent pain is more severe and difficult to control. In addition there is now evidence that suggests that these are not a durable solutions. We have however used this approach in patients in whom definitive adequate surgery has failed. The

introduction of EUS guided nerve blocks requires further evaluation before being incorporated in routine practice.

Surgical treatment of pain in CP should only be considered when other causes of the pain have been excluded and after adequate attempts at medical therapy have failed. There is a long menu of surgical procedures to choose from for the surgical treatment of CP: drainage procedures, resection procedures and a combination of the two.

Lateral pancreaticojejunostomy (LPJ): This is a relatively simple operation, early pain relief is good but falls off with time and eventually only 50-80% of patients remain pain free. It has the advantage of a low morbidity and mortality (<5%).Because there is no resection of pancreatic parenchyma there is a small new endocrine and exocrine insufficiency rate. The role of this procedure should decrease, and be replaced by combination procedures.

Cysto-enterostomy: Following this procedure for CP, recurrence of the inflammatory cyst and ongoing pain occurs in 20-50% of cases. Thus the pathology in the underlying pancreas should be addressed rather than only the cyst itself.

Proximal resections, Pancreaticoduodenectomy(PD): In 20-40% of patients a sclerosing form of the disease is found with a non-dilated duct. In these patients duct drainage procedures are not appropriate. In many series for CP the need to exclude malignancy is the main indication for surgery in up to 43%. Even with intraoperative ultrasound and fine needle aspiration cytology we find that malignancy cannot always be unequivocally excluded and that resection is required. The operation has the advantage of excluding malignancy. The results for pain relief are good with 80% pain free at 5 years.

Distal Resections; Localized fibrosis is unusual in CP especially in the body and tail . Distal pancreatectomy has been shown to be a poor operation with high recurrence rates for pain . There is also a high incidence of new diabetes related to the predominance of *beta* islet cells in the tail.

Total pancreatectomy: Total pancreatic resections are still described. The results for pain relief are poor possibly because by the time this operation is performed the pain is neuronal or central in origin. In addition patients may develop brittle diabetes with rapid onset of diabetic ketoacidosis and coma. With more modern insulin preparations it has been demonstrated that the management of diabetes in patients following TP is not worse than in other type 1 diabetics. Newer enzyme replacement therapies are also improved and as such the management of the exocrine insufficiency is improved.

Combination procedures

Duodenal preserving resections of the head of the pancreas (DPRH): In the late 1980's Beger described the duodenal preserving resection of the head. The results of this operation showed it to be similar to that of PD with respect to pain control but with a lower morbidity rate. As it involves a lesser resection and preserves gastrointestinal continuity, the functional results are better and nutritional status is preserved. This procedure has been reported with long follow-up periods (>5 years) and has also been compared in randomized trials to the PD as well as other duodenal preserving resections. In all these studies it has consistently been shown to have good results with durable pain relief in more than 80%. This operation also manages the complications in neighboring organs: It addresses the narrowing in the distal common bile duct due to fibrosis and can relieve duodenal obstruction.

Local Resection of the head of the pancreas and lateral pancreatico-jejunostomy (LR LPJ): Charles Frey reported a variation of the DPRH, which also involves a lesser resection of the head of the pancreas, and in addition includes a lateral pancreatico-jejunostomy to decompress the ductal hypertension in the remaining gland. This operation involves coring out of the head of the pancreas leaving a narrow rim of pancreatic capsule on the duodenum and on the posterior aspect of the head.

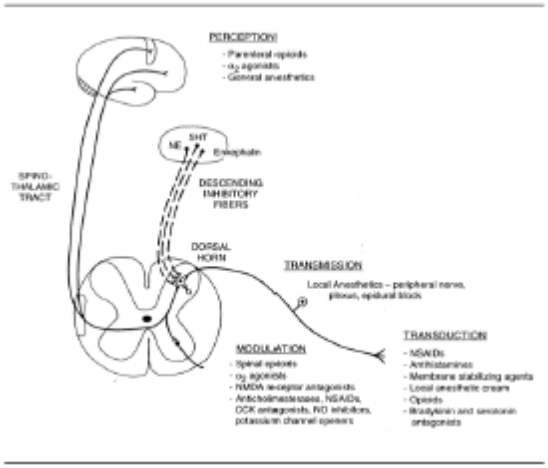
There have been a number of randomized trials comparing the duodenal preserving operations with the Pancreatico-duodenctomy. Besides a lower early morbidity with the duodenal preserving operations, the long term outcomes for pain relief and quality of life are similar for all. As such the decision as to which procedure to choose should be an institutional and individual surgeon preference.

Surgery is able to meet most of the aims of treatment as mentioned above: pain relief, improved quality of life and the exclusion of malignancy. The preservation of function remains an ongoing challenge as it may be hastened by the operation or the natural history of the disease itself. Today the operation of choice for CP in my unit is the Frey LR LPJ, with PD reserved for patients in whom malignancy cannot be excluded.

LOCALIZING PAIN

Dr Dwayne Möhr
Specialist Anaesthetist

While anesthesia is safer than ever before, every person scheduled for a procedure or surgery must have a serious conversation with their physician anesthesiologist about their anesthesia care delivery plan ahead of time. This must include a multifaceted pain management plan.



Post-operative pain affects millions of patients worldwide and the post-operative period has high rates of morbidity and mortality. Some of this morbidity may be related to analgesics. The later should serve as motivation to seek out and employ methods to at least decrease the dose of commonly used systemic drugs, if not totally eliminate their use altogether.

Pain physiology is excruciatingly complex yet a simple scheme of the available targets for therapy, make is simple to see that one cannot rely on only one intervention.

Invasive operations – its accompanying pains and potential complications – gave early modern surgeons and surgery a somewhat negative reputation. Surgeons belonged to an ignoble profession, one joke noted, because they made a living “by the hurts of other men.” Nineteenth century medical practitioners were able to call on general anaesthesia, but some individuals and specific indications such as minor surgery called for an alternative approach. The introduction of cocaine in 1884 completely changed common practice.

Virtually all surgical procedures are amenable to local anaesthesia. This may include any target, from the neuraxis all the way down to the nociceptive receptors at the locus of tissue injury.

We require 100% of clinical efficacy and thus we need to use a dose that will provide this.
Efficacy rather than the potency of a local anaesthetic must be considered.

The main purpose of stating maximum doses is to prevent the administration of excessive amounts of drug, which could result in systemic toxicity.

The maximum doses recommended at present usually do not take into consideration the site of injection and factors which may influence tissue redistribution, metabolism or excretion. And these doses are nearly nonsensical.

Several points must be considered when choosing between different drugs with a similar clinical profile, including the efficacy, safety profile and the costs of the drug.

From a clinical point of view, it seems clear that both the "new" molecules provide a long-lasting block, with a clinical profile very close to that provided by racemic bupivacaine, especially when high concentrations.

Only relevant advantage of these new agents remains the reduced potential of toxicity as compared to bupivacaine.

Discuss the possibility of block techniques with your anaesthesiologist and share the benefits with your patients.

FLUID THERAPY IN SEPTIC PATIENTS: CRYSTALLOIDS OR COLLOIDS; WHICH, WHAT PRODUCT, WHEN AND HOW MUCH? PART I: CURRENT PERSPECTIVE ON FLUID AND ELECTROLYTE HOMEOSTASIS.

JP Pretorius, MBChB MMed(Surg) FCS(SA) Critical Care
Adjunct Professor, Head: Clinical Unit Critical Care, Medical School
Faculty of Health Science, University of Pretoria, Steve Biko Academic Hospital

Introduction.

All living things evolved from the sea – humans as well. Water and electrolytes therefore form the very essence of our being. A frivolous approach to our very innermost composition and daily functional existence leads to mismanagement of fluid and electrolyte therapy in seriously ill patients – patients in whom the nature of the disease itself can afflict fluid and electrolyte homeostasis as well.
Fluid and electrolyte therapy forms the basis of the physiological support of any surgical patient. It cannot be delegated to the most junior member in the medical team, as too often happens – it needs constant expert supervision.

INDICATIONS FOR FLUID AND ELECTROLYTE THERAPY IN SURGICAL PATIENTS

TOTAL FLUID MANAGEMENT: TFM	MAINTENANCE	RESUSCITATION	REPLACEMENT
1. Indication:	Daily requirements	Hypovolaemia	Abnormal or continuing losses.
2. Intention:	According to a formula based on body mass	"Aggressively" according to endpoints	Collect drainage for 4 hours, replace a % during next 4 hours, while collecting again.....
3. Infusion rate:	Continuously per 24 hours = 24 equal doses	Bolus	Continuously according to losses.
4. Type of fluid:	Maintenance: Maintelyte 5%, Electrolyte No2 10% Sustenance 5%	Volume expander: Ringers Lactate (Modified), Plasmalyte B, Saline, Colloids	According to fluid lost: Rehydration solution, 5% Dextrose in water, 0,45% NaCl, 0,9% NaCl, Ringers Lactate
5. Monitor	Serum and urine electrolytes & osmol. Fluid balance chart.	Central haemodynamics, Stroke Volume Variation, Urine flow, SvO_2, Lactate, pH, BE	Serum and urine electrolytes & osmol

- My personal practice and teaching over many years.
- Van Regenmortel, Jorens, Malbrain, Curr Opin Crit Care 2014, 20:390-

The three basic indications for fluid and electrolyte therapy in surgical patients are resuscitation, maintenance and replacement of on going losses – each with its own indication, intention, type of fluid, rate of infusion and monitoring. (1)

WE CAN NO LONGER DENY OR IGNORE THAT FLUID AND ELECTROLYTE THERAPY CONSTITUTES DRUG THERAPY!

No ideal resuscitation fluid exists. Evidence is available that the type, dose and timing of administration of resuscitation fluids matter with regards to outcome. All resuscitation fluids can contribute to the formation of interstitial edema. This is worse under inflammatory conditions - especially if resuscitation fluids are administered excessively. Resuscitation fluids should be considered in the same way as any other intravenous drug. The fluid to be used should be selected according to indications, contraindications and potential toxic effects in order to maximize efficacy and minimize iatrogenic toxicity (2)

Shock occurs when the circulatory system fails to maintain adequate cellular perfusion. Inadequate cellular oxygen utilization is the end result. Fluid therapy is only one component of a complex haemodynamic resuscitation strategy for patients in shock. (2, 3, 4)

The problem of shock during Sepsis.

Septic shock is primarily a form of distributive shock. It typically has ineffective tissue oxygen delivery (DO2) and extraction (VO2) with inappropriate peripheral vasodilation despite preserved or increased cardiac output. A complex interaction occurs between pathological vasodilation, relative and absolute hypovolemia, myocardial dysfunction and altered blood flow distribution due to the inflammatory response of infection. Despite intravascular volume resuscitation, microcirculatory abnormalities may persist and cause maldistribution of cardiac output. (3)

Physiological principles for resuscitation

Any fluid can be harmful if administered inappropriately. Philippus von Hohenheim said in the sixteenth century “All things are poison and nothing is without poison; only the dose permits something not to be poisonous.”(5) Greater amounts of fluids are deleterious for kidney function, causes interstitial edema with increased diffusion distance and worsening of tissue oxygenation. Hypervolaemia leads to secretion of atrial natriuretic peptide which damages the endothelial glycocalyx and result in increased endothelial permeability and increased interstitial edema.
In trials on fluid resuscitation clearly defined hemodynamic endpoints such as haematocrit should be chosen to determine the amounts of fluid administered. Clear guidelines concerning the dosage of fluids for individual patients are not always provided. (5)

Optimal target endpoints for fluid therapy during resuscitation remain controversial. Functional hemodynamic measures (stroke volume variation or pulse pressure variation, bedside ultrasonic interrogation of respiratory variation in inferior vena cava diameter, cardiac output or end tidal CO2 changes associated with passive leg raising) can better predict the hemodynamic response to fluid loading than static metrics of resuscitation like CVP.(6)

It is also only a half-truth to proclaim a more restrictive therapy to be superior to a liberal one. Today rather an adequate and timely replacement of actual losses with appropriate preparations seems to be an ideal primary approach. Crystalloids to replace fluid losses (insensible and urine) based on a protocol, and a goal directed approach to replace volume losses with a colloid. (7)

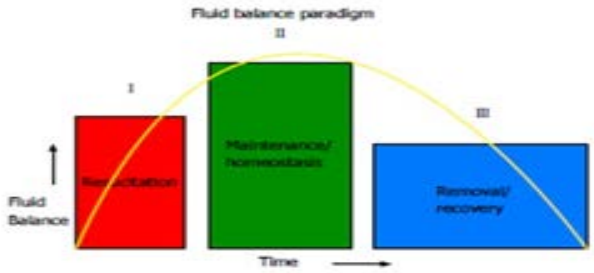


Figure 1
Fluid balance paradigm. The management of fluid therapy in critical illness can be conceptually viewed across three broad phases differentiated according to clinical status of the patient. During the "resuscitation" phase, the goal is restoration of effective intravascular volume, organ perfusion and tissue oxygenation. Fluid accumulation and a positive fluid balance may be expected. During the maintenance phase, the goal is maintenance of intravascular volume homeostasis. The broad aim here would be to mitigate excessive fluid accumulation and prevent unnecessary fluid loading. During the recovery phase, passive and/or active fluid removal would correspond to organ recovery.

A novel conceptual framework for fluid management in critical illness introduces the idea of three interrelated phases of fluid management namely:

a) Acute resuscitation - to restore effective circulating blood volume, organ perfusion and tissue oxygenation. Fluid accumulation and appositive fluid balance may be expected.
b) In the second phase - maintenance of intravascular homeostasis, preventing excessive fluid accumulation by avoiding unnecessary fluid loading.
c) In the final stage fluid removal is the aim. Active de-resuscitation during a state of physiological stabilization, organ injury recovery and convalescence. (6)

The kidney remains our greatest ally in the fluid and electrolyte war. In patients with sepsis-associated acute kidney injury (AKI) continued fluid loading did not improve kidney function. Fluid accumulation was found to be a predictor of 60 day mortality. (6) Monitoring fluid balance is extremely important – especially the cumulative balance in addition to daily fluid balance.

The great ado in the literature to point out the dangers of the starches in order to safe guard our patients has not conclusively proven that products like Voluven and Volulyte should be abandoned. Hydroxyethyl starch (HES) should only be used early and in limited volumes for the acute resuscitation of critically ill hypovolaemic patients. It seems that this was not always the case. It is also not only HES which has renal toxicity – saline has been shown to have serious toxicity too. Iatrogenic hyperchloraemic metabolic acidosis occurs commonly. Bolus administration of saline causes decrease in renal blood flow and renal cortical perfusion leading to an increased incidence of AKI and renal replacement therapy (RRT) There is also evidence that hyperchloraemia worsens the inflammatory response. (6)

IF HES MUST GO, SALINE SHOULD GO AS WELL (Abnormal or unphysiological saline?

Little mention is made of the fact that in the United Kingdom 10 million litres and in the United States 200 million litres of saline are used annually! What is the amount of damage resulting from this in comparison to the damage from the use of HES?

Physiological monitoring as a tool to assess the haemodynamics of shock and to dictate resuscitation

1. What is wrong with the CVP? Aggressive supportive measures may be harmful in critically ill patients. The “Less is more” paradigm may apply. Despite current teaching from the Early Goal Directed Therapy (EGDT) trial, the Surviving Sepsis Campaign recommendations and others there are no human data to show that large volume resuscitation reliably improves organ perfusion. These guidelines use the CVP of 8-12 mm Hg as a target. A high CVP increases venous pressure , increase organ interstitial pressure and reduces organ and microcirculatory flow. In septic patients the Frank-Starling curve is shifted downwards and to the right. They thus show a diminished response to fluid loading.

2. The Frank-Starling curve

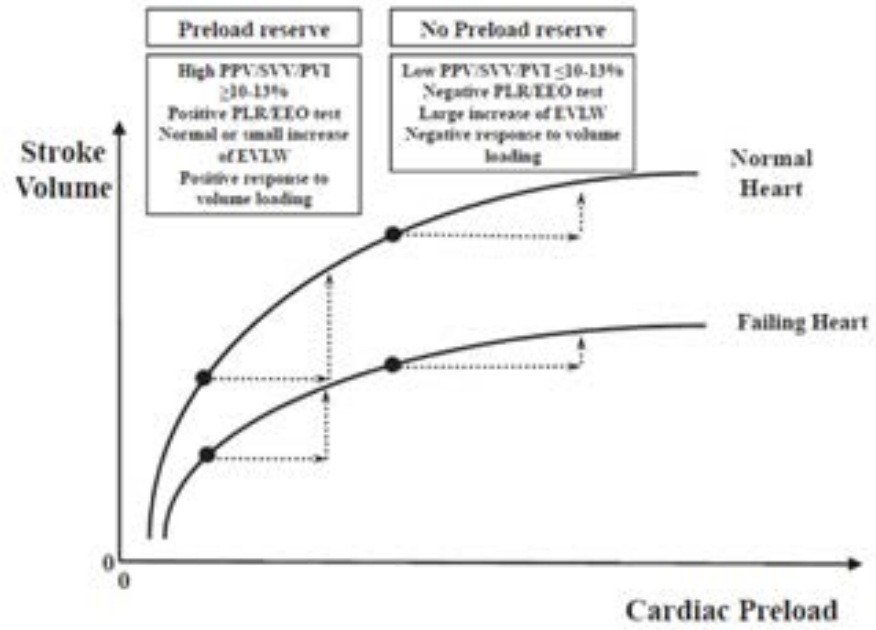
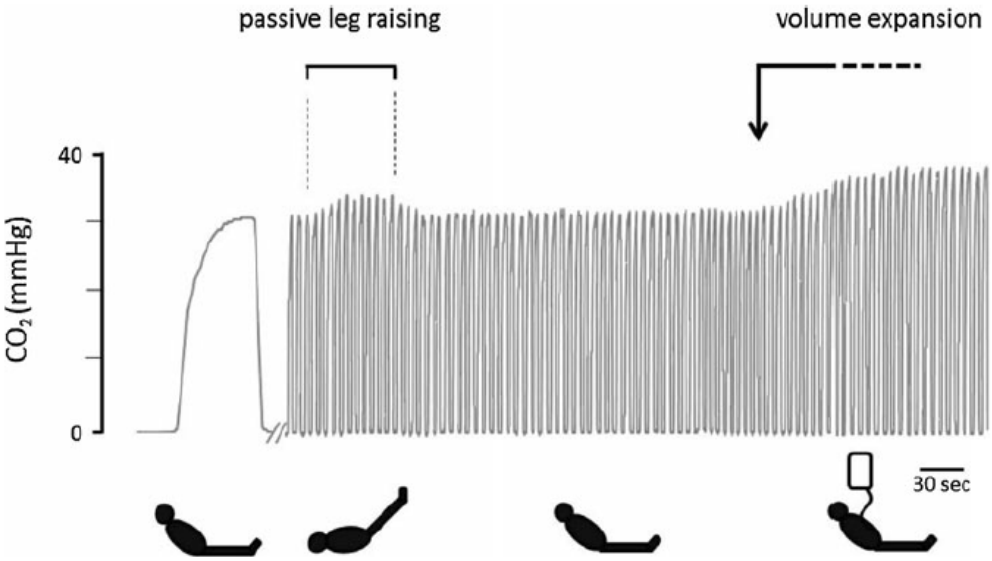


Fig. 1. Frank-Starling curves are influenced by ventricular contractility. There is preload reserve when the ventricle is functioning on the steep part of the curve. This indicates preload responsiveness, where pulse pressure variation (PPV), stroke volume variation (SVV) and pulse variability index (PVI) are high, and end-expiratory occlusion (EEO) and passive leg raise (PLR) tests are positive. Volume loading induces a significant increase in stroke volume, and results in a small increase in extravascular lung water (EVLW). When the ventricle is functioning near the flat part of the curve, there is no preload reserve. This indicates preload unresponsiveness, where PPV, SVV and PVI are low, and EEO and PLR tests are negative. Volume loading has little effect on stroke volume and leads to a large increase in EVLW. (Reproduced with Permission from Ref. [65]) [70].

The concept of preload responsiveness is clearly understood when considering the basic physiology. It is essential to find patients who will increase their cardiac output when receiving fluid. Remember less than 50% of septic cases with hypotension will do so. (8) Excellent monitoring equipment is available to demonstrate this clinically but measurements like stroke volume and pulse pressure variation is affected by spontaneous ventilation and arrhythmias.

The passive leg raise test combined with monitoring the effect on cardiac output or end tidal CO2 (EtCO2), is useful as an indication of preload sensitivity and to guide fluid therapy which should be administered as small boluses of a balanced crystalloid to treat hypovolaemia..



3. The microcirculation is becoming more and more attractive as part of hemodynamic monitoring during fluid resuscitation. This is made possible by the third generation handheld microscope, the Cytocam which allows direct observation of the microcirculation of the floor of the mouth. Dysfunction of the microcirculation is highly correlated with adverse outcome.

<u>Fluids as anti-shock drugs</u>

The Drugs:

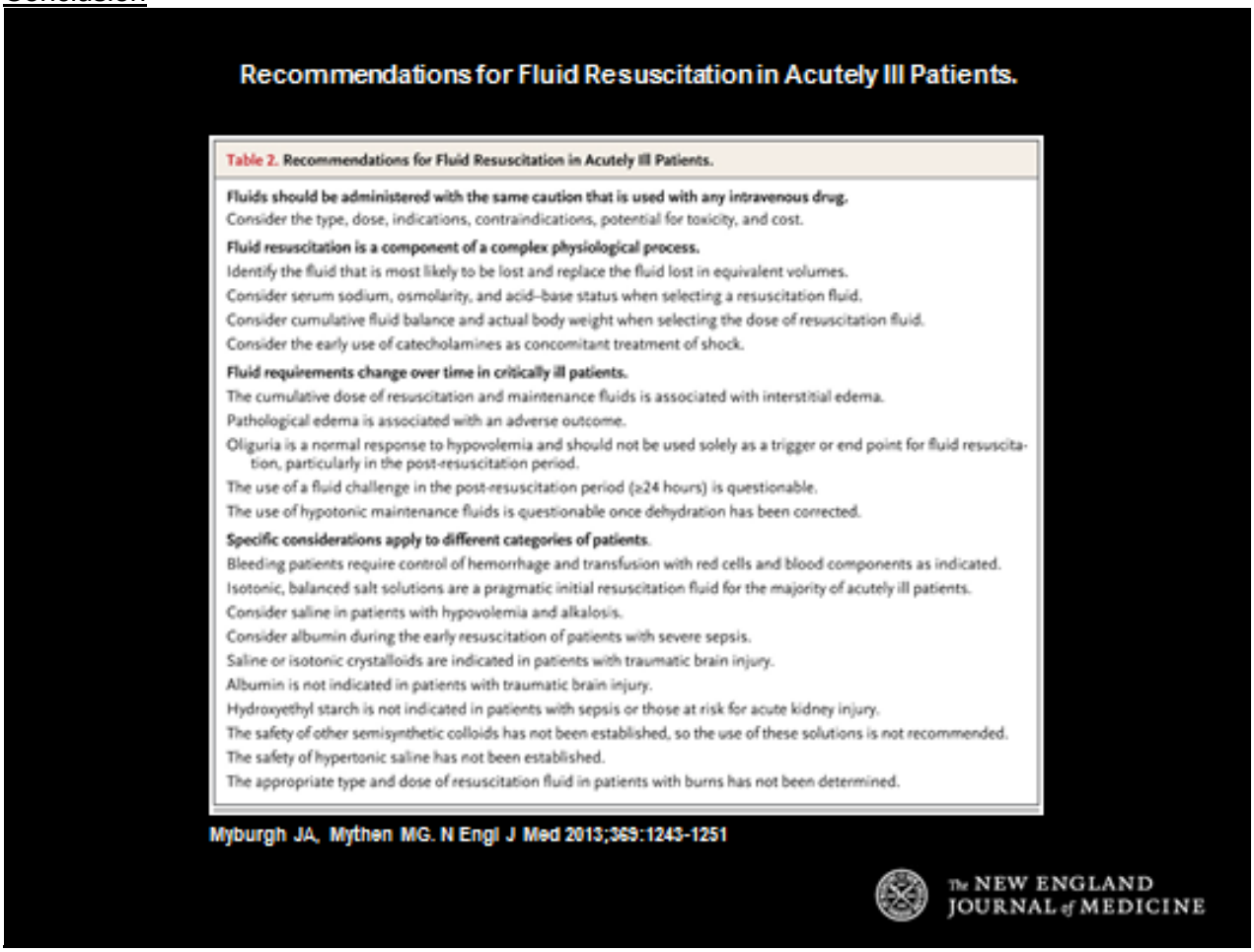
HES
Saline
Ringers lactate
Plasmalyte B
Albumin
Lyophylised plasma in future?

The perfect fluid for shock treatment has not yet been developed.
Only enough is enough. Avoid both too little and too much. Ban conservatism…it will lead to too little.

Meticulously refill the (sacred) intravascular volume then STOP, BUT continue monitoring – the pathophysiological process is on going and fluid may be lost continually.

Volume is necessary – but the question is where to direct the fluid to. Clearly the microcirculation is the target organ of the future. This should be the endpoint.

Conclusion



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FLUID THERAPY IN SEPTIC PATIENTS: CRYSTALLOIDS OR COLLOIDS; WHICH, WHAT PRODUCT, WHEN AND HOW
PART II: SYNTHESISING THE LATEST LITERATURE AND TAKE-HOME MESSAGE

Dr Timothy Hardcastle, MMed(Chir); FCS(SA); PhD; Trauma Surgery (HPCSA)
Trauma Surgery Program and Trauma Intensive Care Service: IALCH and Department of Surgery, University of KwaZulu-Natal, Durban. South Africa

INTRODUCTION

This overview article covers the clinical application of recent advances in the understanding of fluid therapy for the patient with sepsis and septic shock and will aim to place the role of the crystalloids and modern colloids into perspective, in light of the glycocalix theory that has been recently proposed. The overview will conclude with an attempt at presenting a practical approach to fluid selection and administration along with a critique of the 2012 surviving sepsis guideline. This overview is to be read in conjunction with the document concerning the pathophysiology and pharmacology or fluids, as well as modern aspects of volume-status determination, by Prof J Pretorius.

Background

The debate has raged long and hard around the issue of fluid types and volumes of fluid therapy for patients with various pathologies and largely the literature is confusing in that many of the papers combine patient groups, pathologies and age ranges with distinctly different outcomes, yet try to make a single conclusion around the preferred fluid type or volume to be administered. This has led to confusion among emergency specialists, surgeons and intensivists regarding what fluid to use and when to use it, and in what dose.

Literature overview: Recent RCT's examining fluids, sepsis and outcomes.

There have been a number of large recent randomised trials (1-4) examining the effect of fluid therapy on various outcome markers. These trials have included varied numbers of septic patients and varied numbers of surgical patients. The trials have either examined the use of modern colloids versus saline or versus some form of Ringer's Solution (Lactate or Acetate).

The first trial to be published was the CRYSTMAS study (1), a small RCT including 196 patients in two arms, examining HES130/04 (Voluven®) versus NaCl in septic patients with Septic Shock. Patients with pre-existing renal dysfunction or high-dose inotropes were excluded. More than 50% of both groups were pulmonary sepsis, and less than 30% had a surgical pathology. They demonstrated that total quantity of study drug infused over four consecutive days, ICU and hospital LOS, and area under the curve of SOFA score were comparable. There was no difference between AKIN and RIFLE criteria among groups and no difference in mortality, coagulation, or pruritus up to 90 days after treatment initiation. They therefore concluded that less volume of colloid was required for stability to be achieved and that (despite being underpowered) there was no obvious renal compromise (no changes in renal biomarkers).

The second study reported was 6S from the Scandinavian Group (2). They included 798 septic patients and showed a small mortality difference ($p=0.03$) and "need for renal replacement" difference ($p=0.04$) in the group receiving high dose starches, although the absolute numbers were not really that great. Also in each group only 1

patient was still in need for RRT at 90 days. The starch used was a product with a Ringer's Acetate base and not saline. Of note only about 30% of the total cohort was surgical patients and most of these were elderly with emergency surgery (27-29%). While the number of patients requiring RRT was higher in the Starch group, there was NO overall difference in the incidence of AKI between the two groups (35% and 36% respectively). Of note, more patients in the starch group required transfusions (P=0.003), implying (at least to my mind) a sicker group (since this was sepsis and not trauma). Also, there was not a statistically higher bleeding rate in those who got colloids. This apparent conflict of results is not addressed in the paper. Given that the Kaplan-Meyer curves only deviate after day 28 suggest that the assignment of blame to the colloid alone is not really an entirely fair assessment.

The third, and by far the largest, RCT was the CHEST study (3), conducted mainly in Australasia. They randomised 7000 patients to either Voluven® or Saline for all "resuscitation" volumes for up to 90 days post-randomisation. A major problem with this study is the time to randomisation was many hours after admission and no consideration was taken of the fluids during emergency care (Time from ICU admission to randomization — hr 10.9±156.5 and 11.4±165.4 respectively). They found there was no significant difference in mortality in six predefined subgroups.

Renal-replacement therapy was used in 7.0% in the HES group compared to 5.8% in the saline group (relative risk, 1.21; 95% CI, 1.00 to 1.45; P = 0.04). In the HES and saline groups, renal risk and injury was less in the colloid group (P = 0.005), and RIFLE-F was not statistically different (P = 0.12). HES was associated, overall, with significantly more "adverse events" (5.3% vs. 2.8%, P<0.001), although most of these were minor, with no difference in serious adverse events. Of note in this study there were more surgical patients and a better mix of emergency versus elective cases. However, it is important to note that: All other aspects of patient care, including maintenance fluids and nutrition, cardiovascular monitoring, pharmacologic support, and respiratory ***and renal support***, were conducted at the discretion of the treating clinicians, thus the difference in use of RRT between the two groups was not really "randomised" or controlled on this aspect where there was a "statistically significant" apparent difference. There was also no difference in duration of RRT between the groups.

Finally, the fourth, and most widely representative trial, published in 2013, was the CRISTAL study from the Annane group (4), which was a different trial in that the patient groups were stratified and it was open label, but blinded to outcome assessment, thus better reflecting real-world practice. From ICU's in 5 countries a total of 2857 patients were randomised to either colloids or crystalloid resuscitation. No prior fluid resuscitation was allowed, thus addressing the problem with the two previous studies. Additionally the maximum dose of colloid was 30ml/kg, much lower than the prior studies. Only 30% of the patients were surgical and less than 5% overall was trauma. Most patients were septic (54% in each group). The outcomes examined were as for the other two trials. The findings of this pragmatic study included: Less deaths at 28 days (25.4%) in colloids group vs the crystalloids group (27.0%) (relative risk [RR], 0.96 [95%CI, 0.88 to 1.04]; P = .26) and at 90 days, (30.7 vs 34.2%), P = .03. Renal replacement therapy not used more in either group.

Patients in the colloid group had less ventilator days and less fluid overall (P = .01) and more patients without vasopressor therapy by 7 days (P = .04) and by 28 days (P = .03). Interestingly 90-day mortality was lower among patients receiving colloids. The outcome of this study conflicts with the previous two large studies, but was designed with a more every-day practice scenario and thus may more accurately reflects a real situation. Overall the study appeared to favour colloids. Resuscitation

with colloids was associated with more rapid weaning from life-support treatments as shown by significantly more days alive without mechanical ventilation or vasopressor therapy. In this trial, there was no evidence for a colloids-related increase in the risk for renal replacement therapy.

A critique (5) of the former two studies and one older study was published recently and this review highlights the following issues: i) VISEP compared ringer's lactate to 10% HES 200/0.5 in septic patients and found an increased incidence of renal failure in HES receivers. Unfortunately, study treatment was started only after initial stabilization with HES, randomizing hemodynamically stable patients into a rational (crystalloids) and an irrational (high dose starch until ICU discharge) maintenance treatment. ii) 6S compared ringer's acetate to 6% HES 130/0.42 for fluid resuscitation in septic patients and found an increased need of renal replacement therapy and a higher mortality in the HES group. However, patients of both groups were again randomized only after initial stabilization with colloids, the actual comparison was, therefore, again rational vs. irrational. Beyond that, the documentation is partly fragmentary, leaving many important questions around the fate of the patients unanswered. iii) CHEST randomized ICU patients to receive saline or 6% HES 130/0.4 for fluid resuscitation. Actually, despite being reported in a different way, this trial actually showed no relevant differences in outcome. Therefore, two studies showed what happens to septic patients if starches are used in a way not used routinely in practice. The third one actually proved safety. The benefit of perioperative goal-directed preload optimization using starches is therefore unquestioned. Additionally, the last comment by the critique author is reinforced by the results of CRISTAL, published after the critique was written.

Putting Surviving Sepsis (6) into perspective!

The 2012 update to the guideline has the following major recommendations regarding fluid therapy: Early aggressive fluid therapy, using crystalloids, and (if needed) albumin aiming for a 30ml/kg volume and mean arterial pressure of 65mmHg and CVP of 8-12mmHg. Source control is advocated within 12 hours of diagnosis if surgical pathology is identified. They recommended against the use of HES on the basis of VICEP (which used older starches), CHEST (which did not randomise the RTT group) and CHRYSTMAS (which was underpowered to examine renal outcomes) and make the point that the most real-world trial (CRISTAL) was "not considered"! They also support the use of Albumin despite the SAFE trial finding of "no benefit". They also advocate for Hb 7-9g/dl based on the TRIC study, which specifically excluded shocked patients requiring resuscitation, while most authorities still advocate for at least 10g/dl in this context.

The problem with the Guidelines is that they do not consider the other advantages in surgical sepsis offered by the colloids, most of which are not examined in any of the mentioned trials, namely the incidence of Abdominal Compartment Syndrome and surgical anastomotic breakdown. Studies in animals from Iceland (7), Canada (8), and Germany (9,10) all demonstrated a lower anastomotic leak rate with colloids, specifically HES products. This finding was subsequently confirmed in humans in studies from Russia (11), the USA (12) and Germany (13). This is an aspect of particular concern to us as surgeons, who may have performed a bowel anastomosis or repair as part of the source control surgery in septic patients.

Is this all there is? An appraisal of the Glycocalix theory and the influence of Starches.

Already back in 2006 it was suggested that “evidence indicates that using crystalloids exclusively may cause overloading of the interstitial compartment with considerable negative sequelae, whereas using colloids may improve microperfusion and tissue oxygenation” (14) Studies have shown an improvement in endothelial glycocalix function with less aggressive fluid strategies and in fact HES or plasma has been shown to repair impaired glycocalix in sepsis and shock, both in animal and in human studies. (15-18) Saline was shown in the human studies to worsen microcirculatory flow (16, 18). Since the microcirculation is an important new concept it is wise to appreciate the role of the glycocalix in the response to resuscitation of the septic patient, especially the impact of colloids on the rate and extent of the recovery thereof and the subsequent improvement in tissue oxygenation, the ultimate goal of resuscitation.

Where does this leave us in practice?

Marik (19) recently published a review in Annals of Intensive Care, where he emphasised that the Surviving Sepsis guidelines are flawed in recommending the CVP values suggested, as well as potentially excluding colloids, based on the 6S and CHEST trials, while excluding CRISTAL. Additionally he emphasised the serious renal and systemic side effects of saline over other balanced salt-solutions on both the circulation and renal function, especially in light of the volumes required to achieve euvolaemia. A review from 2010 (20) highlighted that the modern colloids appear to have advantages on the microcirculation that to date remain indistinctly defined and that these may be beneficial in the long-run.

Conclusion

In summary, the role of fluids in the septic patient is not in dispute, however the fluid type and volume administered should be guided by microcirculatory markers, which appear to be more clearly defined with the following practical recommendations for daily practice: Fluids are drugs and as such must be used as any other drug, with caution and a balance of risk and benefit. The Colloids appear to have a distinct role as an early goal-directed resuscitation fluid for hypovolaemia, especially in light of the effect on the microcirculation, guided by lactate levels, while crystalloids appear to be better for ongoing fluid support, given that the effect of accumulation appears to hold some long-term problems for both gelatins and HES. It appears as though the concerns about apparent renal impairment and the risk of an increased mortality is overemphasised and not really substantiated by in-depth assessment of the trial results, especially with the two largest and most recent trials. HES remain a safer alternative to the Gelatins, albeit with a greater risk of minor and non-fatal adverse events compared to crystalloids. For us as surgeons the advantages of less tissue oedema and less anastomotic leaks is a fundamental point that requires consideration and further study.

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PRINCIPLES OF DAMAGE CONTROL IN TRAUMA

L.M. Ntlhe, Department of Surgery, University of Pretoria and Steve Biko Academic Hospital

TORSO TRAUMA

INTRODUCTION

Damage Control Surgery (DCS) or abbreviated surgery has gained widespread practice in the last 20 years and has become the standard of care in a select group of multi trauma patients. Uncontrollable haemorrhage which significantly contributed to the high mortality in severely injured patients necessitated this evolution. Damage Control Resuscitation (DCR) which includes DCS has taken also over the last 10 years and intensivists contribute immensely in this regard. This strategy is practiced not only in the abdomen but chest, limbs, head and neck, orthopaedics, vascular, ophthalmology.

Damage control concept originates from the US Navy in the early 1900s. A damaged ship would undergo a quick temporary emergency repairs and injured personnel rendering the ship stable enough to reach port for definitive repair. Military advances have translated to civilian benefits and vice versa, eg ATLS adapted to BATLS Ships US Navy .

Stone and his colleages were the first to describe the technique of " truncated laparotomy" for patients with clinically evident coagulopathy in 1983,Rotondo et.al popularised the term damage control.

Definition

Damage Control Surgery : an abbreviated or bail- out surgical technique with major emphasis of arresting haemorrhage and contamination with minimal regard to anatomical reconstruction. The goal is to avoid mortality from metabolic or physiological failure which occurs in this select group of patients. Early total care has a prohibitively high mortality. (1,2,3)

Damage Control Resuscitation continued rewarming in theatre includes DCS and occurs ideally in an ICU setting, where rewarming, including in the theatre, restrictive fluid administration and recommended blood component transfusion ratios of : 1 : 1 : 1 – blood, plasma, platelets guided by validated massive transfusion protocols are provided(4)

The metabolic exhaustion, which resulted in many patients' death is avoided by limiting surgery to arresting haemorrhage and contamination

i) Torso : part of the body to which the neck and limbs are attached
ii) Damage control surgery – abbreviated or "bail-out" surgery
iii) Damage control resuscitation includes DCS

PATHOPHYSIOLOGY:-

HYPOTHERMIA

Haemorrhage leads to hypothermia and impaired tissue perfusion further leads to an inability to generate heat, sympatho- adrenal overstimulation leads to vasoconstriction educing tissue blood flow and oxygenation even more. Mortality increases from 40% to 100% when core temperature decreases from 34^0 to 32^0 (Jurkovich et al) Hypothermia in trauma victims: Ominous prediction of survival. J Trauma 1987; 27: 1019-24

Hypothermia results in dysrythimas, impaired myocardial contractility and cardiac output, left shifts the oxygen Hb dissociation curve preventing oxygen off-loading to the cells.

Clotting cascade disruption develops due to slowed-down temperature sensitive enzyme-activated serine esterases, platelet dysfunction ,endothelial abnormalities (Sagraves, Toschlog & Rontondo) leading to reduced thromboxane B2, which results in inhibition of platelet aggregation – NB - replacement platelets also become dysfunctional. Fibrinolytic systems is also altered.(3,4)

ACIDOSIS

Shock results in anaerobic metabolism, resulting in lactic acidosis. Lactate clearance as a marker of successful resuscitation , is widely accepted. Abrahamson et al obtained a 100% survival with a 24-hour lactate clearance compared to 14% survival if lactate was not cleared in 24 hours.

Acidosis causes redused patients response to both endogenous and exogenous catecholamines resulting in "uncoupling of β adrenergic receptors Adrenergic response worsens cellular acidosis by direct effects in the cel.

COAGULOPATHY

Two mechanisms

(a) Delusional due to aggressive IV fluid resuscitation
(b) Consumptive coagulopathy
    1) Due to tissue factor release coagulation activation.
    2) ? Protein C activation resulting in Plasminogen Activator inhibition

(PAI – 1)resulting in Inhibition of clotting cascade, added systemic anti-coagulation and hyper fibrinolysis

DAMAGE CONTROL SEQUENCE

a) Part I: in OR,
Interventional radiology

b) Part II: ICU

Correction of acidosis
Correction hypothermia
Correction of coagulopathy

- IV fluid and blood products, rewarming techniques, ventilation and pulmonary recruitment, pharmacotherapy, including inotropes
- Unplanned re-operations

c) Part III: definitive surgery
Definitive closure (2,3)

PATIENT SELECTION(1,2)

Table 1. Damage Control: Key Factors in Patient Selection

Conditions
High-energy blunt torso trauma
Multiple torso penetrations
Hemodynamic instability
Presenting coagulopathy and/or hypothermia
Complexes
Major abdominal vascular injury with multiple visceral injuries
Multicavitary exsanguination with concomitant visceral injuries
Multiregional injury with competing priorities
Critical factors
Severe metabolic acidosis (pH <7.3)
Hypothermia (temperature <35°C)
Resuscitation and operative time >90 minutes
Coagulopathy as evidenced by development of nonmechanical bleeding
Massive transfusion (>10 units packed red blood cells)

Adapted from Rotondo MF, Zonies DH. The damage control sequence and underlying logic. *Surg Clin North Am.* 1997;77:761.

TORSO TRAUMA OPERATIVE TECHNIQUES AND SEQUENCE

The torso can absorb high energy impact from all angles. The front, back, sides, from above and below, with devastating consequences.
Mechanisms of injury: blunt, penetrating, blast

THORACIC: Majority of these injuries end up being definitive ops because of exsanguination.

LUNG:-

Exsanguinating haemorrhage

1)DeBakey clamp to hilum
2)twist the hilum to kink the major hilar vessels

Tractotomy or pulmonotomy, use a linear stapling cutting device to expose and ligate bleeders (NON- ANATOMIC approach recommended)
Suture the tracts with absorbable sutures

Finger occlusion and suture over pledges

Significant ruptures may clamp the SVC & IVC AND (to avoid cardiopulmonary bypass) suture rapidly when the heart slows down.

Air is vented out before clamps are removed.

ABDOMEN:

LIVER

Early decision essential and experience is key
Adequate mobilization of the liver is important
Pringle manoeuvre precedes: finger fracture

1)Hepatomy & selective vascular ligation or

2)Resectional debridement & vascular ligation

Packing is highly recommended in most severe cases to avoid coagulopathy or if present ab initio

SPLEEN
Splectomy for AAST injury grade3, 4, and 5
Grades 1and 2 may be sutured or repaired with a absorbable mesh bag

PANCEATICO-DUODENAL, SMALL AND LARGE BOWEL
Major injuries are best treated by drainage and a feeding jejunostomy
No place for elaborate surgery
Haemostasis should however be secured , may necessitate packing

MAJOR ABDOMINAL VESSELS
Arteries
Options : ligation, lateral suture and in experienced hands interposition grafts for infra-renal aortic injuries should in these be discovered in theatre
SM Vein, Common &Ext Iliac may ligate, infra –renal IVC LIGATE & Bilateral 4 quadrant fasciotomy if in PROFOUND shock

DAMAGE CONTROL RESUSCITATION

REWARMING:
Warm icu, ivf, warming devices, wet clothes removed
Aim for at temperature of 37 Degrees in 4 hours or else active rewarming eg pleural warm normal saline
Ventilatory circuit should be warm
Ventilation techniques adjusted accordingly, with recruitment in mind
COAGULATION CORRECTION:
Stop haemorrhage it may entail an unscheduled theatre trip including haemostatic resuscitative compounds. (3,4,5)

	Mode of delivery (commercial examples)
Factor concentrators*	
Mineral zeolite	Granules (QuikClot); mesh bags (QuikClot Sport Advanced Clotting Sponge); gauze (QuikClot Combat Gauze)
Biological polymers	Powder (TraumaDex); nylon bags (self-expanding haemostatic polymer)
Mucoadhesives†	
Chitosan	Granules (TraumaStat); gauze (Chitogauze PRO, Celox, Hemogrip)
Chitin	Gauze (Modified Rapid Deployment Hemostat)
Mineral-based	Granules (WoundStat, WoundSeal Powder)
Synthetic peptides	Powder (InstaClot)
Polyethylene glycol	Gel (Coseal)
Oxidised cellulose	Gauze (BloodSTOP, Surgicel Fibrillar, Surgicel Nu-Knit)
Gelatin	Foam (Sugifoam, Gelfoam, Gelfilm)
Microfibrillar collagen	Powder (Avitene Flour, Helitene, Instat); rolled sheet (Avitene Sheets, EndoAvitene); sponge (Avitene Ultrafoam, Avitene Ultrawrap, Helistat); gel (Vitagel)
Procoagulant supplementors‡	
Human-derived factors§	Dry: oxidised cellulose and polyglactin matrix with thrombin and fibrinogen coating (Fibrin Pad); gauze imbedded with lyophilised fibrinogen and thrombin (Dry Fibrin Sealant Dressings); equine collagen patch with fibrinogen and thrombin (TachoSil) Liquid or aerosol: fibrin sealants (Tisseel, Evicel, Crosseal); gelatin–thrombin suspension (Floseal)
Bovine-derived factors¶	Gauze (FastAct); glue (BioGlue); sponge (TachoComb)
Plant-derived factors	Powder (HemoStase MPH, Arista)
Synthetic factors¶	Solution (Recothrom)

The appendix lists the manufacturers of all products. *Rapidly absorb water from blood to concentrate factors that promote clot formation. †Adhere to tissues and form a physical barrier to seal bleeding wounds. ‡Deliver procoagulant factors to bleeding wounds to promote clot formation. §Examples include fibrinogen, thrombin, calcium, and coagulation factor XIII. ¶Examples include thrombin.

Table 2: **Topical haemostatic agents**

Factor vii vs Traneximic acid
Cryoprecipitate administration until fibrinogen levels are100mg/dL
Restrictive crystalloid administration
Whole blood v/s ratio of 1:1:1 for rbc: plasma: platelets
Blood transfusion guided by validated protocols(7,8)

INTENSIVE HAEMOSTATIC MONITORING ESP TEG utilization
Cardiovascular monitoring including Swan-Ganz pulmonary catheterization to asses cardiac output and appropriate actions taken

Constant search for organ deterioration and compartment hypertension
Pharmacotherapy including inotropes
Ideal Staffing with a 2:1 nurse /patient ratio

ACIDOSIS CORRECTION:
This usually corrects itself as soon as the patient is volume replete and warm and the patient has reverted to aerobic metabolism.
Sodium Bicarbonate is rarely required unless the pH is < 7.1 or < 7.2

COMPLICATIONS OF DAMAGE CONTROL :
1) Compartment Hypertension and syndrome

Abdomen
Chest
Intracranial
Extremeties

2)Sepsis
3) Enteric fistulae
4)Wound dehiscence
5)Hernias
6) ICU RELATED complications

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PRINCIPLES OF DAMAGE CONTROL SURGERY: VASCULAR SURGERY

S.C Tsotetsi: MBChB, MMed (UFS), FCS(SA), Cert. Vascular(SA)

Vascular trauma is a major cause of significant morbidity and mortality with the highest rates of death from thoracic aortic transections and major abdominal venous injuries. Risk factors, diagnosis, and management considerations vary depending on the vessel injured. However, in general, early diagnosis and intervention are paramount for improving the likelihood of a favourable outcome. Isolated vascular injury is more common with penetrating mechanisms and prognosis is generally more favourable in these cases. In contrast, vascular trauma from blunt mechanisms is often found in patients with complex multisystem injuries, which can result in both delays in diagnosis and competing management principles.

Damage control surgery (DCS) is an operative strategy that sacrifices the completeness of the immediate surgical repair in order to address the physiological consequences of the combined trauma of the injury and surgery. In the past this has been very much focused on abdominal trauma and the idea of performing an 'abbreviated laparotomy'. However the concepts are applicable to injury beyond the abdomen, including the management of wounds, head injuries, maxillofacial trauma and fractures. However, central to DCS is early recognition and management of the physiological consequences of the injury.

The decision to adopt a damage control approach to surgical intervention in a trauma patient should be reached early, in order to avoid the vicious cycle being entered, rather than employing DCS as a measure of desperation. DCS is only applicable to a minority of trauma patients and if used too liberally may be no better or even worse than immediate definitive surgery. However, too strict a definition as to when to adopt the approach, particularly based on laboratory indices, can mean that the adverse physiological consequences are already established. Experience and rapid surgical assessment are key to making a positive, informed decision to adopt a DCS strategy.

Indicators for damage control surgery:

Preoperative	Intraoperative
High-energy trauma Multisystem trauma: major abdominal injury and extra-abdominal injury Systolic blood pressure less than 70 mmHg Coagulopathy Hypothermia e core temperature < 34^0C	Major thoracic or abdominal vascular injury Severe hepatic injuries Severe bowel oedema/bowel ischaemia

Primary suture repair of vessel wall suits clean lacerations of the artery and vein. However it is not suited for complete vessel transection or in the presence of devitalized vessel wall. Ligation of vessels is a simple but effective technique for gaining rapid haemostasis and may be the best option where the access is difficult and complex repairs are time consuming. The subclavian vein, iliac vein and inferior vena cava can be ligated albeit with the risk of limb oedema although this may be life-saving in the context of uncontrolled haemorrhage. The external carotid artery can be ligated with no consequences although internal carotid artery ligation risks neurologic deficits. Ligation of femoral arteries can result in limb ischaemia although subclavian artery ligation may be better tolerated. Temporary shunts ensure distal perfusion through a damaged vessel. This is a temporizing measure until the patient is stable enough to return for complex reconstructive repair after correction of

coagulopathy. Choice of vascular shunts can range from simple endotracheal suction tubing cut to desired lengths to specifically designed vascular shunts such as the carotid shunts. Primary amputation may be the only option to secure expeditious haemostasis in a mangled extremity. This decision is often made by a multidisciplinary team where a patient's haemodynamic instability precludes complex reconstructive repair. Use of Foley catheter tamponade provides for occlusion of both the proximal and distal ends of a bleeding vessel, which, if successful, promotes rapid stabilization on the field before transport to higher echelons of care

Endovascular balloon occlusion for temporary vascular control is also gaining renewed interest. Use has been described recently for penetrating arterial injuries, inferior vena cava control, major hepatic vascular injury, and pelvic exsanguination. The breadth of experience is limited but proponents advocate that it results in reduced bloodloss, especially in difficult exposures, avoids entering the hematoma without proximal control, reduces operative time, and, in select cases, can be paired with endovascular covered stent

Neck injuries

Carotid artery injuries are best managed by primary surgical repair and active bleeding from vertebral artery injury is amenable to angiographic embolization. Endovascular stenting of proximal carotid and innominate artery are less invasive options which can avoid a sternotomy. The internal jugular vein may either be repaired, or ligated with impunity if necessary.

Thoracic injuries

For emergency thoracotomy when the underlying injury has not been defined, an anterolateral thoracotomy through the fourth intercostal space on the side of the injury is the best approach. This incision can be extended across the sternum or into the abdomen as required. When an injury to the central organs of the chest is expected, a midline sternotomy will provide the best access to the heart, the great vessels of the mediastinum and the hila of both lungs. Endovascular repair is often the treatment of choice in traumatic aortic injury.

Endovascular management of subclavian and proximal axillary artery injuries has the potential to simplify treatment of these difficult to access injuries. The first successful case report of ENDO subclavian repair occurred in 2000, with the largest series analyzing 57 patients by du Toit et al. from South Africa. The majority of these cases were stab victims with a false aneurysm managed semi electively.

Abdominal vascular injuries

Exposure of the midline vascular structures requires reflection of the abdominal viscera to the midline from the left or right. Large, right-sided retroperitoneal haematoma or dark blood gushing and not spurting are suggestive of vena caval injury. The exposure of the vena cava and right iliac vessels is achieved by incising the peritoneum lateral to the duodenum and right colon, and medial reflection of the colon and small bowel mesentery. Surgical exposure of these large veins has to be done with extreme care as these vessels are thin walled and liable to tear or result in avulsion of side branches. Venous blood rapidly wells up obscuring the surgical field and control of haemorrhage is often best achieved by compression using swab sticks or simple pinching of the tear to allow for exposure and suturing of the defect. Bright red blood bleeding briskly from the epigastrium or a large haematoma in this region should raise the suspicion of injury to the aorta or its major vessels. Control of the aortic inflow can be temporarily achieved by compressing the aorta against the vertebral body at the aortic hiatus of the diaphragm. Aortic exposure is accomplished by displacing the spleen and colon medially after incising the lateral peritoneal

attachments. The proximal aorta is exposed by dividing the left crus of the diaphragm. Exposure of anterior aorta and proximal trunk requires the kidney to remain posterior during this exposure and medial displacement of the kidney exposes the posterior aorta. The pelvic vessels are best exposed by a lateral approach and displacing the sigmoid colon or caecum medially. Access to the iliac veins is difficult due to the overlying arteries and occasionally may warrant initial division of the iliac artery. This facilitates better visualization of the iliac veins after retracting the divided ends of the iliac artery for repair of the vein. The arterial ends can subsequently be anastomosed to re-establish distal circulation.

Abdominal solid organ injury

Modern radiological imaging and interventional techniques have significantly modified the management of hepatic and splenic injury. Although the haemodynamically stable patient with liver, kidney or splenic injury is managed conservatively, laparotomy is indicated in the unstable patient. Packing can control most haemorrhages related to hepatic injury. Pringle's manoeuvre of clamping the porta hepatis via the hepatoduodenal ligament is a very effective temporizing measure in the control of hepatic arterial or portal vein injury. Where local facilities exist, radiological embolization is the treatment of choice for solid abdominal organ haemorrhage unless haemodynamic instability precludes this. Liver haemorrhage can usually be initially treated by selective embolization of a branch of the hepatic artery within the liver substance, though the delayed complications of infected collections and bile leaks must be subsequently excluded prior to discharge. The majority of splenic lacerations can be treated by conservative management or by embolization and the main splenic artery can be embolized if necessary with subsequent splenic perfusion and function preserved via the blood supply from the short-gastric vessels. The unstable patient with major haemorrhage from splenic injury is an indication for splenectomy. Decisions as to the management of major renal lacerations must balance the increased incidence of nephrectomy in patients undergoing immediate vs delayed surgical exploration, with the increased morbidity of patients who are managed expectantly. The alternative of endovascular treatment is therefore an important and less-invasive option for managing renovascular trauma that may allow for maximum tissue/organ preservation.

Pelvic haemorrhage

Major pelvic haemorrhage is encountered in pelvic fractures and during pelvic dissection in gynaecology, urology, colorectal and vascular surgery. This poses great challenges to the surgeon due to difficulties of access. The mortality associated with pelvic haemorrhage from fractures is high and hence haemorrhage control is critical to improve patient survival. A pelvic sling or belt for fracture stabilization is very effective in controlling haemorrhage in the emergency setting. External fixator devices provide robust stabilization of the pelvis and these can be easily applied in the trauma room. Angiographic embolization of bleeding vessels is the treatment of choice for haemodynamically unstable patients with pelvic fractures. In surgical bleeding from the pelvis, there are various techniques available to control major haemorrhage. A combination of digital pressure and simple suture ligation is often a very effective technique. However, occasionally haemorrhage control may necessitate ligation of major feeding vessel such as the internal iliac artery.

Peripheral arterial injuries (PAIs)

These are the most common vascular injuries encountered in patients with trauma. Despite lower associated direct mortality from PAI, the potential for significant morbidity is high, especially when lower extremity vessels are involved. Although vascular injuries, especially in cases of penetrating trauma, can occur in isolation, they are often present in patients with severely compromised extremities. Extensive

soft tissue loss or bony involvement complicates the decision to attempt vascular repair and is a major factor in the probability of long-term success. The Mangled Extremity Severity Score (MESS) was originally developed as a guide for practitioners when faced with a significantly injured extremity. Patients with MESS scores of 8 or higher were traditionally considered non-salvagable. This definitive cut-off has been recently challenged in the literature, in which functional limb salvage rates of greater than 50% were achieved with rapid revascularization (<5 hours after injury) and liberal use of fasciotomy in patients with a MESS greater than or equal to 8.The use of temporary vascular shunts and tourniquets in the treatment of limb threatening or life-threatening arterial injuries has gained renewed interest because of lessons learned in the Iraq and Afghanistan conflicts. Whereas there are limited data regarding the routine use of endovascular techniques following lower extremity penetrating arterial trauma, selective use of coil embolization has been described by several groups. As expected, arterial embolization is reserved for branch vessel occlusions, most commonly for internal iliac, profunda femoris, or tibial branch bleeding.

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WHEN IS DEFINITIVE SURGERY FOR PEPTIC ULCER DIATHESIS APPROPRIATE AND WHAT PROCEDURE

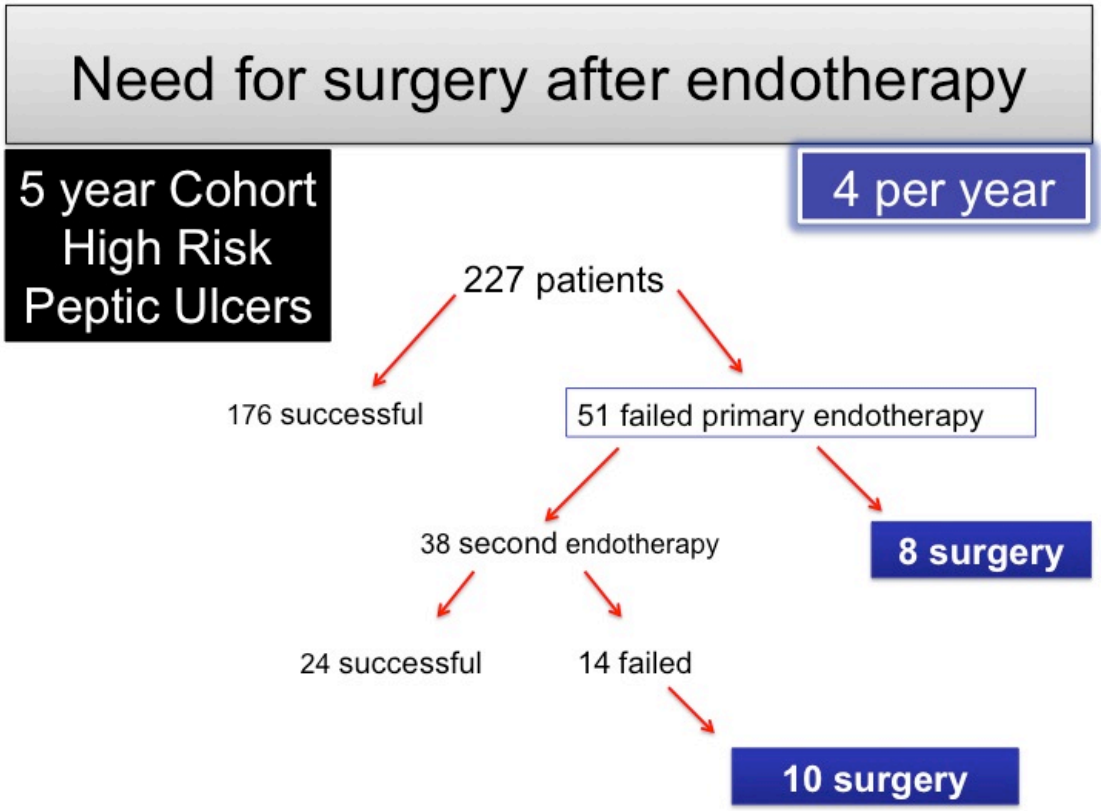
SR Thomson ChM FRCS Eng and Edin and FRCP(Edin)
Head of the Division of Gastroenterology.
University of Cape Town

Introduction: Peptic ulcer disease is now a curable condition. With eradication of H Pylori and effective acid suppression the vast majority of peptic ulcers can be managed, with either short term medication for cure or with continued effective acid suppression to keep the lid on symptoms and prevent the most common complication, bleeding[1-3]. Surgery is now reserved for those with the complications of bleeding (80%) perforation (17%) or gastric outlet obstruction (3-5%). A recent systematic review[4] estimates the annual incidence of peptic ulcer hemorrhage or perforation to be respectively 19.4–57.0 and 3.8–14 per 100,000 individuals with the annual incidence of perforation is on the decline in several countries[4-6]. The main aim in the management of complicated peptic ulcer by surgery is to treat the life threatening complication rather than to effect surgical "cure" of the diathesis via a vagotomy and drainage procedure or a gastric resection. [7-8] The death knell of definitive surgery for peptic ulcer disease was heralded in the British Medical Journal editorial of Sir Alexander Williams in 1991 "Requiem for Vagotomy"[7].

Historical development: Division of the vagi "to cure" peptic ulcer is an operation steeped in surgical history from the time when Pavlov discovered the neural control of gastric secretion[9]. Then followed the Dragsted era of truncal vagotomy and later the concepts of selective and highly selective vagtomy or denervation of the parietal cell mass all designed to minimise the deleterious side effects of truncal vagotomy [10]. These have now largely been relegated to history because of their significant side effect profile (diarrhoea, delayed gastric emptying, bloating, gallstones and nutritional deficits) or simply due to their ineffectiveness in the long term[11]. The effectiveness of medical therapy has developed pari passu with several other advances in surgery, medical gastroenterology and interventional endoscopy. These advances are in intravenous PPI therapy and endotherapy for the management of bleeding ulcers [12], in laparoscopic surgery for the treatment of peptic ulcer perforation [13] and balloon dilatation and stenting to relieve gastric outlet obstruction[14]. These aspects are dealt with sequentially.

Bleeding:
Surgery for acute bleeding is now restricted to patients with an exsanguinating bleed or those in whom endoscopic therapy fails. For bleeding gastric ulcers, a gastrotomy with under-running of the bleeder is for the majority. Local data from a five year study conducted at Groote Schuur Hospital puts into perspective how rarely surgery is required in these patients with only 4 per year requiring an operation[15]. This means the average surgeon in training has very little exposure to this type of surgery and may require experienced help when more than just oversewing of a bleeding vessel in the ulcer base is necessary.

Figure 1



This trend in the reduction of number in patients requiring surgery for complications is confirmed in a large study for the USA[4]. The national estimate of hospitalizations for PUD decreased significantly by 29.9%, from 222,601 in 1993 to 156,108 in 2006 The reduction was 37.2% for duodenal ulcers and 19.6% for gastric ulcers. In comparison to 1993, patients hospitalized for PUD in 2006 more frequently had endoscopic treatment to control bleeding 12.9% vs. 22.2%, underwent fewer gastrectomys 4.4% vs. 2.1% and vagotomys 5.7% vs. 1.7%. Recent data from a Norwegian study on bleeding peptic ulcer disease showed how with improved endoscopic haemostatic techniques, the rate of surgical intervention has dropped from 6.7% in the 1990s to less than 2% in the present day[5].

The move away from definitive surgery has been vindicated by ulcer cure rates in excess of 90% in patients who have had successful H.pylori eradication therapy after control of the bleeding episode.[3] Patients who require long term non–steroidal anti-inflammatory drug (NSAID) therapy are advised to take concomitant PPI medication[16].

Simple patch closure:

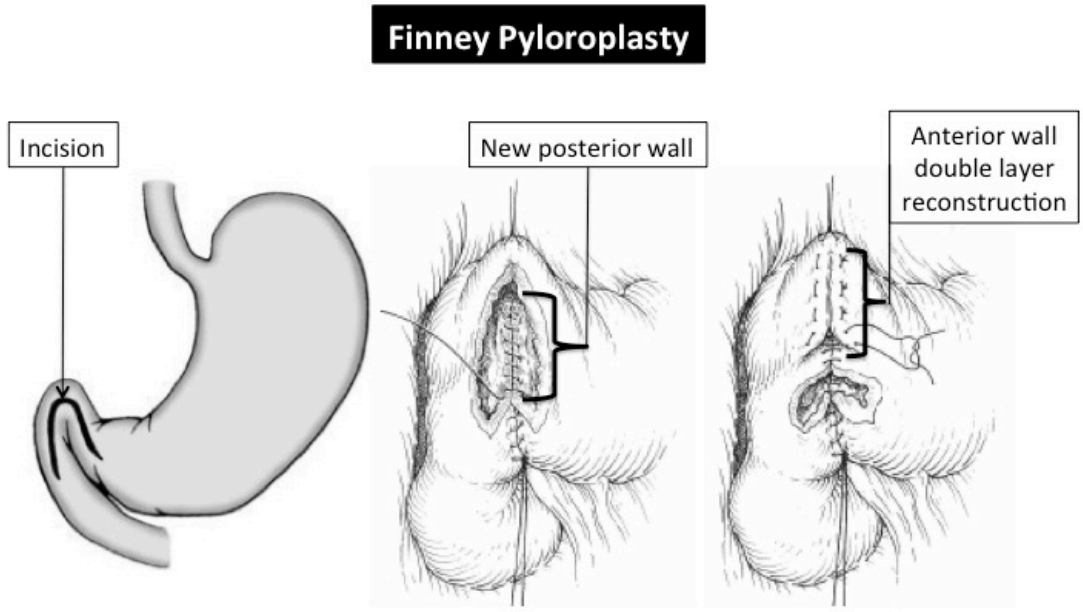
The long debate about the choice between simple patch closure or definitive surgery has been settled in favour of patch closure combined with H. Pylori eradication for duodenal ulcer[2]. This is also true for gastric ulcer perforation[17]. There is conclusive evidence that the risk of recurrent ulceration is below 10% with this combination therapy[3]. Simple patch closure is also the treatment of choice for NSAID-induced perforations since PPI therapy provides effective ulcer protection in these patients. This trend is also evident in a recently published series of 114 patients with perforated peptic ulcer over 6 years period where laparoscopic patch

closure constituted 42% of the operations performed[5]. In this cohort only three patients had a gastrectomy. Gastrectomy is reserved for giant penetrating or perforating ulcers (>5cm in the stomach and >2cm in the duodenum) or when there is a strong suspicion of a malignant ulcer. In this situation the patient co-morbidities and physiological reserves must be factored in to the decision to do more major surgery.

Gastric outlet obstruction: GOO

Previously the surgical treatment for GOO was vagotomy and a drainage procedure or alternatively vagotomy and antrectomy. As with bleeding and perforated ulcers, definitive operations have become less necessary as addressing the obstruction is all that is generally needed after successful eradication of H.pylori. This can be solved by minimally invasive balloon dilitation and stenting [14,16]. Stenting solutions are far more frequently applied to malignant gastroduodenal obstruction where they are highly effective in the short term. However they are by no means perfect and only small series have been reported. In general the main draw back is with migration of the covered stents and then recurrent obstruction[16].Therefore for "*burnt-out ulcers*" with residual fibrotic strictures a Finney pyloroplasty is all that is required in a patient who is fit for surgery.

Figure 2. Modified from Bornman [20]

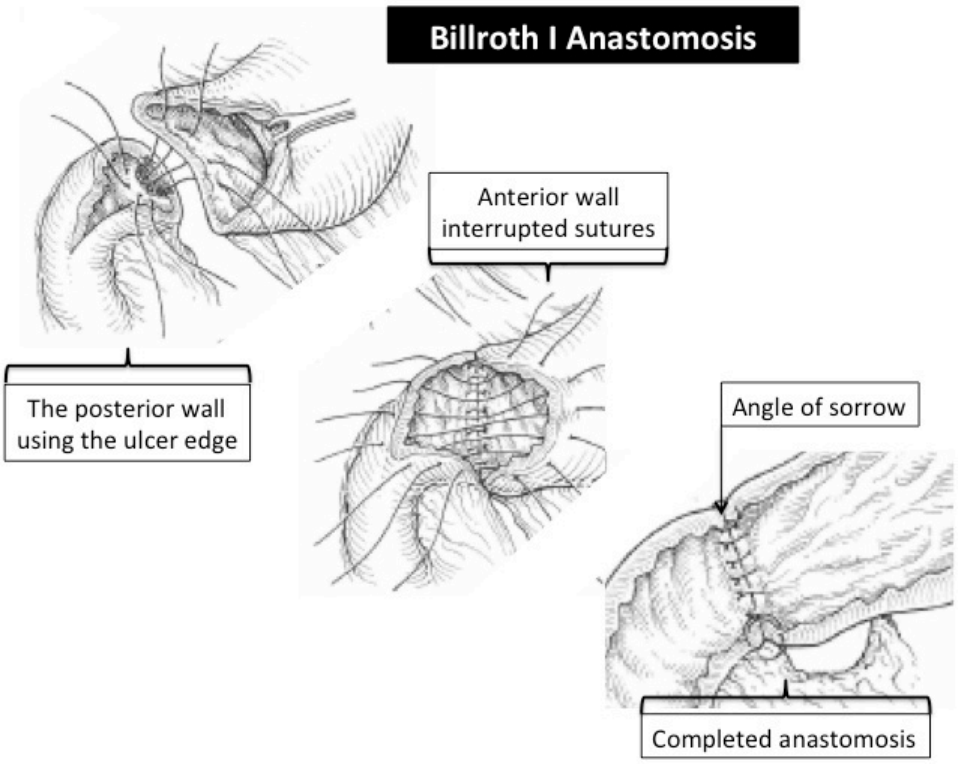


This is the authors preferred operation for burnt out peptic ulcer with gastric outlet obstruction as it creates a wider posterior and anterior lumen.

Recalcitrant Ulcers: A more difficult question is what to offer patients with persistent or recalcitrant penetrating ulcers despite successful H.pylori eradication or those who present with recurrent complications. The reason why these ulcers fail to heal remains uncertain but many of the patients are smokers. This habit contributes to an impaired local healing process which is thought to play an important role in the persistence of the ulcer. A limited distal resection with exclusion of the ulcer should be performed in these situations. Figure 3 Modified from Bornman [20]

Resection when your hand if forced at surgery.

In the emergency situation this is generally when the ulcer is so destructive that the



only safe form of closure is a limited resection gastrectomy. In this situation it is always best to work from inside the ulcer pinching the ulcer tissue from the thickened normal tissue and thence leaving the ulcer base behind but excluding it when continuity is restored. This gastric of duodenal repair does nor lend itself to stapled solutions easily and these reconstructions are best hand sutured. They should generally not involve a vagotomy [18]. I favour a gastroduodenal anastomosis (Billroth I) reconstruction not just for an incisural gastric ulcer but also for a recalcitrant duodenal ulcer or a gastric outlet obstruction. In the situation of a diseased duodenum it is almost always possible after full Kocherisation of the duodenum to spatulate the first-second part of the duodenum to allow and an adequate lumen to construct a duodenogastric anastomosis. The ulcer edge attached to the mucosa is used as the posterior wall using a single layer interrupted anastomosis. As shown in Figure 3.

Summary:

Definitve surgery for peptic ulcer disease should be the exception rather than the rule. Surgery should be tailored to the situation as minimlly invasive methods have application across the three major complications. Gastric resection should be the

procedure of choice when deemed necessary. Those inexperienced with gastrectomy should have senior assistance to deal with the technical challenges.

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EOSINOPHILIC ESOPHAGITIS

Dr FM Potgieter, Gastroenterologist, Pretoria East hospital.

Esophageal eosinophils were once considered to be a hallmark of gastroesophageal reflux disease. However, it has become apparent that the esophagus, which is normally devoid of eosinophils, is an immunologically active organ that is capable of recruiting eosinophils in response to a variety of stimuli.
Eosinophilic esophagitis (EoE) is defined as "a chronic, immune/antigen-mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation"

EPIDEMIOLOGY

EoE has been reported in most countries.
Higher prevalence in temperate zones than in tropical climate zones[1]
The incidence of eosinophilic esophagitis appears to be increasing[2]
Incidence has increased by 0.35 per 100,000 population between 1991 and 1995 to 9.45 per 100,000 between 2001 and 2005.[3]
Majority of affected adults have been men in their 20s or 30s

Mean age at diagnosis was 34 years (range 14 to 77 years)[4]
Symptoms (predominantly dysphagia) had been present for an average of 4.5 years prior to diagnosis.
Male predominance may be related to variations in a gene located on the X-chromosome.
Significantly more likely to be Caucasian (84 percent compared with 73 percent.)

NATURAL HISTORY

In one study of 30 untreated patients followed for an average of 7.2 years, dysphagia persisted in 29 (97 percent). During follow-up, symptoms increased in 23 percent, were stable in 37 percent, and decreased in 37 percent. Attacks of dysphagia occurred more frequently in patients with blood eosinophilia or with pronounced findings on endoscopy.[5]

CLINICAL MANIFESTATIONS

1
Prevalence of esophageal eosinophilia varies by climate zone in the United States
Hurrell JM, Genta RM, Dellon ES
Am J Gastroenterol. 2012;107(5):698.

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Eosinophilic esophagitis: escalating epidemiology?
Straumann A, Simon HU
J Allergy Clin Immunol. 2005;115(2):418.

3
Epidemiology of eosinophilic esophagitis over three decades in Olmsted County, Minnesota.
Prasad GA, Alexander JA, Schleck CD, Zinsmeister AR, Smyrk TC, Elias RM, Locke GR 3rd, Talley NJ
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Clinical and endoscopic features of eosinophilic esophagitis in adults.
Croese J, Fairley SK, Masson JW, Chong AK, Whitaker DA, Kanowski PA, Walker NI
Gastrointest Endosc. 2003;58(4):516.

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Natural history of primary eosinophilic esophagitis: a follow-up of 30 adult patients for up to 11.5 years.
Straumann A, Spichtin HP, Grize L, Bucher KA, Beglinger C, Simon HU
Gastroenterology. 2003;125(6):1660.

1. Dysphagia (Most common)
2. Food impaction
3. Chest pain that is often centrally located and does not respond to antacids
4. Gastroesophageal reflux disease-like symptoms/refractory heartburn
5. Upper abdominal pain[6]

A history of food impaction is present in up to 54 percent of patients.[7]
Esophageal strictures have been noted in up to 31 percent of patients.
Esophageal dysmotility may also be observed.
Present in 1 to 4 percent of patients with refractory reflux.[8]

ASSOCIATIONS WITH OTHER DISORDERS

A strong association with allergic conditions such as food allergies, environmental allergies, asthma, and atopic dermatitis. It has been estimated that 28 to 86 percent of adults and 42 to 93 percent of children with eosinophilic esophagitis have another allergic disease.

In one series, 10 of 13 patients (77 percent) had a history of an allergic disorder defined as asthma, allergic rhinitis, urticaria, hay fever, atopic dermatitis, food allergy, or medicine allergy, and/or positive RAST test or positive allergic skin tests [73]. Twelve of 13 patients (92 percent) had an absolute peripheral eosinophilia and 9 of 12 patients (75 percent) had concurrent eosinophilic gastroenteritis.[9]

An association with celiac disease has been reported in multiple studies, and in one series a response to a gluten-free diet was also noted.[10]

In addition, an association with connective tissue disorders, caustic injury, antibiotic exposure in infancy, and a Schatzki ring have also been described, although the strength of the associations is unclear.[11]

DIAGNOSIS

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García-Compeán D, González González JA, Marrufo García CA, Flores Gutiérrez JP, Barboza Quintana O, Galindo Rodríguez G, Mar Ruiz MA, de León Valdez D, Jaquez Quintana JO, Maldonado Garza HJ
Dig Liver Dis. 2011;43(3):204.

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Idiopathic eosinophilic esophagitis.
Vitellas KM, Bennett WF, Bova JG, Johnston JC, Caldwell JH, Mayle JE
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Quaglietta L, Coccorullo P, Miele E, Pascarella F, Troncone R, Staiano A
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Association of Schatzki ring with eosinophilic esophagitis in children.
Nurko S, Teitelbaum JE, Husain K, Buonomo C, Fox VL, Antonioli D, Fortunato C, Badizadegan K, Furuta GT
J Pediatr Gastroenterol Nutr. 2004;38(4):436. Pharmacol Ther. 2007;26(3):487.

11

The diagnosis of eosinophilic esophagitis should be based upon symptoms, endoscopic appearance, and histological findings. The first diagnostic test is typically an upper endoscopy with esophageal biopsies following two months of treatment with a proton pump inhibitor. In addition, other disorders that can cause esophageal eosinophilia, such as gastroesophageal reflux disease (GERD), should be ruled out.

DEFINITIONS

1. *Esophageal eosinophilia.*

Esophageal eosinophilia is the finding of eosinophils in the squamous epithelium of the esophagus.
Esophageal eosinophilia can be seen in association with multiple conditions.

- *Gastroesophageal reflux disease (GERD)*
- *Eosinophilic esophagitis (EoE)*
- *Eosinophilic gastrointestinal diseases (EGIDs)*
- *Celiac disease*
- *Crohn's disease*
- *Infection*
- *Hypereosinophilic syndrome (HES)*
- *Achalasia*
- *Drug hypersensitivity*
- *Vasculitis*
- *Pemphigoid vegetans*
- *Connective tissue disease*
- *Graft versus host disease*

2. *Eosinophilic esophagitis*

Diagnostic criteria have been proposed in at least two consensus guidelines. The most recent guideline, issued in 2013 by the American College of Gastroenterology, proposed the following.[12]

- *Symptoms related to esophageal dysfunction*
- *Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of ≥15 eosinophils per high power field*
- *Mucosal eosinophilia is isolated to the esophagus and persists after two months of treatment with a proton pump inhibitor (PPI) trial*
- *Secondary causes of esophageal eosinophilia have been excluded.*
- *A response to treatment (dietary elimination; topical glucocorticoids) supports the diagnosis but is not required.*

The requirement of more than 15 eosinophils as a cut-off has not been extensively validated. It is possible, for example, that patients with lesser degrees of esophageal eosinophilia after treatment with a PPI may still respond to treatment for eosinophilic esophagitis.

12
ACG clinical guideline: Evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE).
Dellon ES, Gonsalves N, Hirano I, Furuta GT, Liacouras CA, Katzka DA, American College of Gastroenterology
Am J Gastroenterol. 2013;108(5):679.

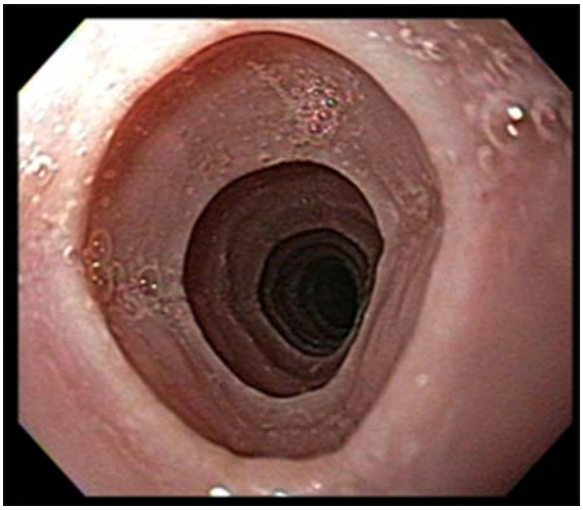
3. *PPI-responsive esophageal eosinophilia*

Patients with clinical and histologic features compatible with eosinophilic esophagitis but who respond histologically to a PPI have been described as having PPI-responsive esophageal eosinophilia. The pathogenesis of esophageal eosinophilia in such patients is not well understood. Interestingly, PPIs block STAT6, which is involved in binding of the eotaxin-3 promoter in esophageal epithelial cells, suggesting that the response to PPIs in some patients may in part be due to an anti-eosinophil effect.[13]

ENDOSCOPIC FINDINGS

A 2012 meta-analysis that compared 4678 patients with eosinophilic esophagitis and 2742 controls estimated the frequency of the following endoscopic features.[14]

- *Stacked circular rings ("feline" esophagus): 44 percent*
- *Strictures (particularly proximal strictures): 21 percent*
- *Attenuation of the subepithelial vascular pattern: 41 percent*
- *Linear furrows: 48 percent*
- *Whitish papules (representing eosinophil microabscesses): 27 percent*
- *Small calibre esophagus: 9 percent*



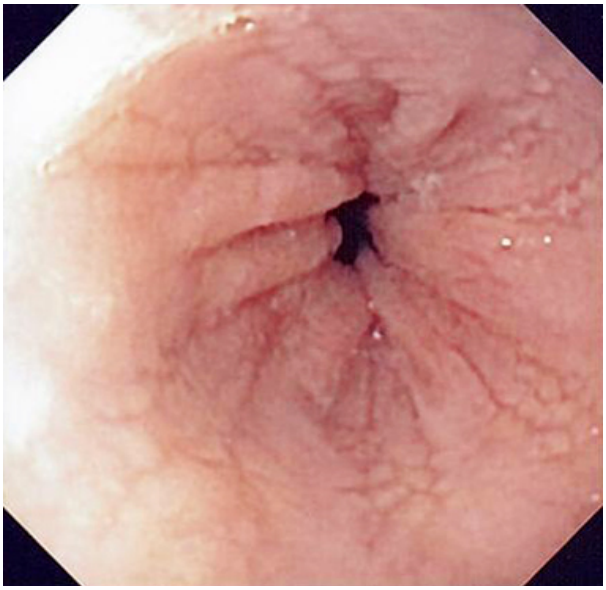
Endoscopic picture depicting the "feline esophagus"

13

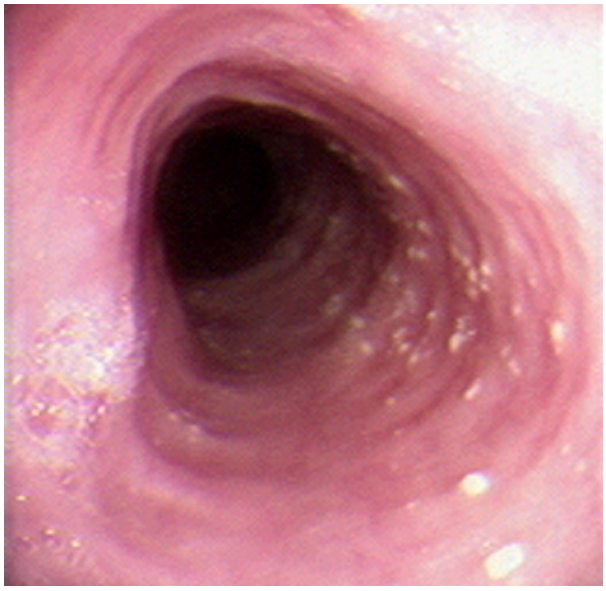
Omeprazole blocks STAT6 binding to the eotaxin-3 promoter in eosinophilic esophagitis cells.
Zhang X, Cheng E, Huo X, Yu C, Zhang Q, Pham TH, Wang DH, Spechler SJ, Souza RF
PLoS One. 2012;7(11):e50037. Epub 2012 Nov 21.

14

The prevalence and diagnostic utility of endoscopic features of eosinophilic esophagitis: a meta-analysis.
Kim HP, Vance RB, Shaheen NJ, Dellon ES
Clin Gastroenterol Hepatol. 2012;10(9):988.



Endoscopic picture showing linear furrows



Endoscopic picture depicting white papules

Individual endoscopic features suggestive of eosinophilic esophagitis had low sensitivity ranging from 15 to 48 percent but high specificity ranging from 90 to 95 percent. Positive and negative predictive values ranged from 51 to 73 percent and 74 to 83 percent, respectively. Given the low sensitivity of endoscopic findings for eosinophilic esophagitis and variable positive predictive value, histology remains important in making a diagnosis of eosinophilic esophagitis, regardless of the endoscopic appearance.

HISTOLOGY

Esophageal biopsies from patients with eosinophilic esophagitis show an increased number of eosinophils. The vast majority of patients have at least 15 eosinophils per high power field (peak value) in at least one biopsy specimen after taking a proton

pump inhibitor. Esophageal eosinophilia in the absence of clinical features is not sufficient to make a diagnosis of eosinophilic esophagitis.[15]

During endoscopy biopsies should be obtained from the distal esophagus as well as either the mid or proximal esophagus.[16]

The sensitivity of biopsies for diagnosing eosinophilic esophagitis depends upon the number of biopsies obtained:

A study found that the sensitivity for two, three, and six biopsies was 84, 97, and 100 percent, respectively.[17]

It has been recommended that two to four biopsies be obtained from the distal esophagus, as well as another two to four from the mid or proximal esophagus. Biopsy specimens should be fixed in formalin.

Other histologic findings suggestive of eosinophilic esophagitis include.

- *Eosinophil microabscesses*
- *Superficial layering of eosinophils*
- *Sheets of eosinophils*
- *Extracellular eosinophil granules*
- *Subepithelial and lamina propria fibrosis and inflammation*
- *Basal cell hyperplasia*
- *Papillary lengthening*
- *Increased numbers of mast cells, B cells, and IgE bearing cells.*

RADIOLOGY

Barium studies are not sensitive for diagnosing eosinophilic esophagitis, but can help characterize anatomic abnormalities and provide information on the length and diameter of strictures.
Findings described in patients with eosinophilic esophagitis undergoing barium studies include strictures and a ringed esophagus. (See picture)

15

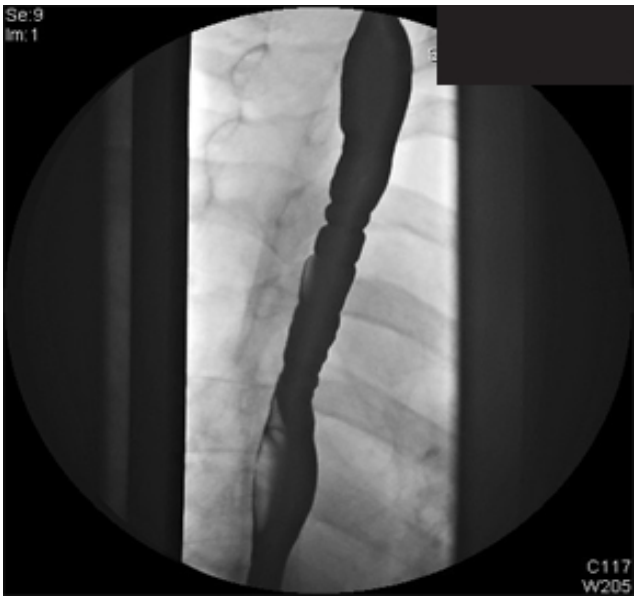
Low grade esophageal eosinophilia in adults: an unrecognized part of the spectrum of eosinophilic esophagitis?
Ravi K, Talley NJ, Smyrk TC, Katzka DA, Kryzer L, Romero Y, Arora AS, Alexander JA
Dig Dis Sci. 2011;56(7):1981.

16

Histopathologic features of eosinophilic esophagitis.
Collins MH
Gastrointest Endosc Clin N Am. 2008;18(1):59.

17

Histopathologic variability in children with eosinophilic esophagitis.
Shah A, Kagalwalla AF, Gonsalves N, Melin-Aldana H, Li BU, Hirano I
Am J Gastroenterol. 2009;104(3):716.



LABORATORY TESTS

50 to 60 percent of patients with eosinophilic esophagitis will have elevated serum IgE levels (>114,000 units/L). Peripheral eosinophilia is seen in 40 to 50 percent of patients but is generally mild. It decreases with topical glucocorticoid therapy.[18]

EVALUATION FOR ALLERGIES

It is suggested that patients with eosinophilic esophagitis undergo evaluation by an allergist or immunologist.

DISTINCTION FROM GERD

The most common consideration in the differential diagnosis of eosinophilic esophagitis is GERD. As noted above, large numbers of eosinophils (>100/HPF) may be seen in association with GERD.
In a study of 712 patients with upper gastrointestinal symptoms undergoing endoscopy, 35 (5 percent) had ≥15 eosinophils/HPF on biopsies obtained from the upper-middle esophagus. Twenty-six patients (75 percent) had a clinicopathologic remission on treatment with a PPI, including half of the patients with a typical eosinophilic esophagitis phenotype. Based upon these findings, the authors concluded that using histologic criteria alone to diagnose eosinophilic esophagitis may lead to an overestimation of the prevalence of the disorder.[19]
Because of the association of GERD with esophageal eosinophilia, biopsies for eosinophilic esophagitis should be obtained after two months of treatment with a PPI or after an esophageal pH study has excluded reflux.
Histologic features suggestive of eosinophilic esophagitis rather than GERD include:

18
Atopic characteristics of adult patients with eosinophilic esophagitis.
Roy-Ghanta S, Larosa DF, Katzka DA
Clin Gastroenterol Hepatol. 2008;6(5):531.

19
Esophageal eosinophilic infiltration responds to proton pump inhibition in most adults.
Molina-Infante J, Ferrando-Lamana L, Ripoll C, Hernandez-Alonso M, Mateos JM, Fernandez-Bermejo M, Dueñas C, Fernandez-Gonzalez N, Quintana EM, Gonzalez-Nuñez MA
Clin Gastroenterol Hepatol. 2011;9(2):110.

Large numbers of intraepithelial eosinophils on histologic examination. In two reports, the presence of more than 20 eosinophils/HPF was typically associated with non-acid-related causes of esophagitis and patients with eosinophilic esophagitis had significantly more eosinophils than patients who responded to therapy for GERD (28 to 31 versus 5 per HPF overall, and 19 to 32 versus 1 per HPF with biopsies from the proximal esophagus). Patients with eosinophilic esophagitis are also more likely to have ≥15 eosinophils/HPF in three or more biopsies taken at different levels.
Other histologic findings favouring eosinophilic esophagitis include proximal esophageal involvement, subepithelial and lamina propria fibrosis, eosinophilic abscesses, more severe basal cell hyperplasia, activated mucosal mast cells/increased epithelial tryptase density, and degranulating eosinophils.
Assessment of eotaxin-3 and major basic protein (MBP) levels in esophageal biopsy specimens (by immunohistochemistry or real-time PCR) has been suggested to help differentiate GERD from eosinophilic esophagitis, but further studies are needed.

TREATMENT OF EoE:

Treatment consists of dietary, pharmacological, endoscopical and experimental therapies.

1.DIETARY THERAPY
Dietary therapy is an effective first-line treatment for eosinophilic esophagitis in children and adults.

1.1 DIETARY TREATMENT OPTIONS

1.1.1 ***Testing-directed elimination diet*** –Skin prick testing (SPT) and atopy patch testing (APT) are performed to test for food allergies, with subsequent elimination of foods with positive test results (plus cow's milk because of its poor negative predictive value on testing).

1.1.2 ***Empiric elimination diet*** – The empiric elimination diet is based upon the concept that the empiric avoidance of those foods that most commonly cause immediate hypersensitivity in a population, such as the majority of immunoglobulin E (IgE)-mediated food reactions (i.e., milk, egg, soy, wheat, peanuts/tree nuts, fish/shellfish). This is called the six-food elimination diet (SFED). However, accumulating data shows that fish/shellfish and peanuts/tree nuts are rare triggers for EoE, and foods such as grains and meats are more common triggers.

1.1.3 ***Elemental diet*** – The patient is placed on an elemental formula, which eliminates all potential food allergens.

2.PHARMACOLOGIC THERAPY

2.1 ***Acid suppression***
PPIs may benefit patients with esophageal eosinophilia either by reducing acid production in patients with co-existent GERD, or by other yet undefined anti-inflammatory mechanisms.
Approximately one-third of patients with suspected eosinophilic esophagitis have a good clinical and histologic response to PPIs alone, suggesting that GERD, or a PPI-responsive form of esophageal eosinophilia, may be responsible.[20]

20
Comparison of esomeprazole to aerosolized, swallowed fluticasone for eosinophilic esophagitis.
Peterson KA, Thomas KL, Hilden K, Emerson LL, Wills JC, Fang JC

In a randomized trial, 42 patients with newly diagnosed eosinophilic esophagitis were randomly assigned to treatment with aerosolized swallowed fluticasone (440 mcg twice daily) or esomeprazole (40 mg daily) for eight weeks followed by an upper endoscopy with biopsies. In patients without coexisting GERD, there was no significant difference in resolution of esophageal eosinophilia between the esomeprazole and fluticasone treatment arms (18 versus 24 percent). In contrast, among patients with GERD, those treated with esomeprazole were significantly more likely to have resolution of esophageal eosinophilia as compared with fluticasone (100 versus 0 percent).[21]

2.2 *Topical glucocorticoids*

Most patients with eosinophilic esophagitis respond to topical glucocorticoids as demonstrated by a decrease in eosinophil counts.[22]
Randomized controlled trials have not consistently demonstrated an improvement in dysphagia with topical glucocorticoids.[23]

2.2.1 *Fluticasone propionate*

Fluticasone is administered using a metered dose inhaler without a spacer. The medication is sprayed into the patient's mouth and then swallowed. Patients should not inhale when the medication is being delivered and they should not eat or drink for 30 minutes following administration.

The optimal dose has not been established. A general approach is based upon the patient's age.

Patients ≥11 years of age (including adults): 220 mcg inhaler, two sprays twice daily. A 2013 guideline issued by the American College of Gastroenterology (ACG) suggested that the dose in adults can range from 880 to 1760 mcg/day in divided doses.[24]

Patients who are destined to respond tend to do so quickly (within one week and often within one to two days). In patients who respond, treatment is given for eight weeks. Patients frequently relapse when treatment is stopped, with reported relapse rates of 14 to 91 percent. For patients who relapse, we treat and discuss maintenance topical glucocorticoids or a trial of a dietary approach. For patients who do not respond to fluticasone, options include a higher dose of fluticasone, a change to oral viscous budesonide, or a dietary approach.

2.2.2 *Budesonide*

Budesonide has been evaluated in case series and randomized trials and appears to be effective for treating eosinophilic esophagitis.[25]

Dig Dis Sci. 2010;55(5):1313.

21

Randomized controlled trial comparing aerosolized swallowed fluticasone to esomeprazole for esophageal eosinophilia.
Moawad FJ, Veerappan GR, Dias JA, Baker TP, Maydonovitch CL, Wong RK
Am J Gastroenterol. 2013;108(3):366.

23

Swallowed fluticasone improves histologic but not symptomatic response of adults with eosinophilic esophagitis.
Alexander JA, Jung KW, Arora AS, Enders F, Katzka DA, Kephardt GM, Kita H, Kryzer LA, Romero Y, Smyrk TC, Talley NJ
Clin Gastroenterol Hepatol. 2012;10(7):742.

24

ACG clinical guideline: Evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE).
Dellon ES, Gonsalves N, Hirano I, Furuta GT, Liacouras CA, Katzka DA, American College of Gastroenterology
Am J Gastroenterol. 2013;108(5):679.

25

In a randomized trial, 36 adults and adolescents with active eosinophilic esophagitis were randomized to budesonide 1 mg twice daily or placebo for 15 days. The budesonide was administered using a nebulizer and patients were instructed to continuously swallow the accumulated liquid. Patients who received budesonide were more likely to have significant improvements in dysphagia compared with those who received placebo (72 versus 22 percent).[26]

3. *Topical versus systemic glucocorticoids*
Systemic glucocorticoids have a limited role in eosinophilic esophagitis.
A randomized trial compared topical with systemic glucocorticoids. The trial included 80 children with eosinophilic esophagitis who were randomly assigned to oral prednisone or swallowed fluticasone. Almost all of the patients, regardless of treatment, were symptom free by four weeks. Histologic improvement was seen to a greater degree in the prednisone group.

MAINTENANCE THERAPY

Maintenance therapy with topical steroids and/or dietary restriction should be considered for all patients, but particularly in those with severe dysphagia or food impaction, high-grade esophageal stricture, and rapid symptomatic/histologic relapse following initial therapy.
In adults, a guideline issued by the ACG suggests a maintenance dose of fluticasone (880 mcg daily in divided doses) or oral viscous budesonide (1 mg daily).

4.Experimental and ineffective therapies.

4.1 ***Antihistamines***- Little benefit has been seen in patients treated with medications aimed at controlling allergies, including antihistamines.

4.2 ***Montelukast***- One series examined eight adults who were treated with montelukast. Six of eight patients had complete symptom relief. However, there was no effect on esophageal eosinophilia. Several side effects were observed, including nausea and myalgias. The safety of the high doses used in this study is unclear.[27]

PROGNOSIS

Untreated, patients may remain symptomatic or have episodic symptoms. Symptoms frequently recur in patients treated with a short course of topical glucocorticoids. The largest study on the natural history in adults focused on 30 adults who were followed for an average of seven years. The majority of patients had persistent dysphagia. Attacks of dysphagia were more common in patients who had peripheral

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Oral viscous budesonide is effective in children with eosinophilic esophagitis in a randomized, placebo-controlled trial.
Dohil R, Newbury R, Fox L, Bastian J, Aceves S
Gastroenterology. 2010;139(2):418.
26

Budesonide is effective in adolescent and adult patients with active eosinophilic esophagitis.
Straumann A, Conus S, Degen L, Felder S, Kummer M, Engel H, Bussmann C, Beglinger C, Schoepfer A, Simon HU
Gastroenterology. 2010;139(5):1526.
27

Eosinophilic oesophagitis: a novel treatment using Montelukast.
Attwood SE, Lewis CJ, Bronder CS, Morris CD, Armstrong GR, Whittam J
Gut. 2003;52(2):181.

eosinophilia. Eosinophilic infiltration persisted in all symptomatic patients, but the degree of tissue eosinophilia appeared to decrease. The inflammatory process remained confined to the esophagus without gastric or duodenal involvement. No cases of dysplasia or esophageal malignancy were observed.[28]

28

Natural history of primary eosinophilic esophagitis: a follow-up of 30 adult patients for up to 11.5 years.
Straumann A, Spichtin HP, Grize L, Bucher KA, Beglinger C, Simon HU
Gastroenterology. 2003;125(6):1660.

RECTAL PROLAPSE

Dr B.H. Pienaar, Department of Surgery, University of Pretoria

The discussion will not refer to paediatric rectal prolapse as spontaneous resolution usually occurs in children in over 90% of cases; surgical management is very rarely indicated.
This condition has been known since the time of Hippocrates (1500 BC).
It is important to distinguish between

1. full thickness
2. rectal mucosal and
3. Internal prolapse (internal intussusception).

The problem in studying the condition is that it can only be done after the problem has established itself.

In 1912 Moschcowitz suggested that the cause was a sliding herniation of the pouch of Douglas into the anterior part of the distal rectum.

In 1968 Broden and Snellman, with defaecography, showed that the condition was really a full thickness intussusception starting approximately 8 cm above the dentate line.

The master concept following the above is that of obstructed defaecation syndrome with tissue laxity.

When both these concepts are evaluated the following common features emerge.

1. Pelvic floor weakness has to be present.
2. There is an indication of herniation.
3. Problematic anal sphincter complex.
    a. Internal (smooth)
    b. External (striated) merging with puborectalis.
4. Anatomical abnormalities in relation to redundancy.

There are two main groups of patients that present with procidentia.

1. Women above the age of 50, with peak incidence above 70 years of age.
2. Males may present as a group under the age of 40 but in association with psychiatric disorders.

Distinguishing anatomical features include

1. Very deep cul de sac (Pouch of Douglas).
2. Anal sphincter abnormality.
3. Diastasis of the levator ani complex.
4. Absence or extreme laxity of the rectal sacral attachment.

It is unclear whether these features are the result or the cause of the problem. Harmston C, Jones OM, Cunningham C, Lindsey I. The relationship between internal rectal prolapse and internal anal sphincter function. *Colorectal Dis*. Jul 2011;13(7):791-5.

A list of predisposing conditions is mentioned but more than 50% of patients give a clear history of longstanding defaecatory difficulty with constipation. Another very common finding is that of neurologic disorders. Although pregnancy might play a role

approximately 35% of cases are found in nulliparous women, but this group presents at a younger age. Wijffels NA, Collinson R, Cunningham C, Lindsey I. What is the natural history of internal rectal prolapse?. *Colorectal Dis*. Aug 2010;12(8):822-30.

The weakness in the pelvic floor that leads to symptoms can be placed in compartments.

1. Anterior (cystocoel),
2. middle (vaginal and uterine),
3. Posterior (rectocoel, enterocoel and rectal).

Rectal prolapse then can either be internal (IRP) or external (ERP) depending on the level of prolapse. The level is determined by the Oxford grading system.

The question of whether IRP will progress to ERP has been cause for debate for a long time as it was noted that IRP did not always progress to ERP,
1. Mellgren A, Schultz I, Johansson C, Dolk A. Internal rectal intussusception seldom develops into total rectal prolapse. Dis Colon Rectum. 1997 Jul;40(7):817-20.

2.Choi JS, Hwang YH, Salum MR, Weiss EG, Pikarsky AJ, Nogueras JJ, Wexner SD. Outcome and management of patients with large rectoanal intussusception.Am J Gastroenterol. 2001 Mar;96(3):740-4.

and indeed IRP was found in up to 50% of volunteers, without any symptoms, with defaecography. Shorvon PJ, McHugh S, Diamant NE, Somers S, Stevenson GW. Defecography in normal volunteers: results

and implications. Gut. 1989 Dec;30(12):1737-49

However, it was shown that the process of rectal prolapse is a gradual continuous process through radiologically identifiable stages with a variable rate of progression. The rate of progression is most likely influenced by anatomical and physiological factors. A strong relationship between age and prolapse grade was demonstrated. The logical deduction must be made that ERP can never be a sudden event, but it can be argued that patients with high grade IRP might be asymptomatic or just diagnosed as ODS. Wijffels NA, Collinson R, Cunningham C, Lindsey I. What is the natural history of internal rectal prolapse?. *Colorectal Dis*. Aug 2010;12(8):822-30.

Symptomatology

Faecal incontinence is the most common symptom, followed by straining, incomplete evacuation (which might explain the incontinence or rather leaking of faecal matter) digital assistance and repeated toilet attendance.
Incontinence can be explained on twofold basis namely

1. Dilated and dysfunctional sphincter and
2. constantly weeping extruded mucosa.

Physical examination

Important to distinguish between mucosal and full thickness prolapse with reference to radial and concentric mucosal folds respectively.
Solitary rectal ulcer may be seen. Decreased anal sphincter tone may be present.

Special investigations

Colonoscopy and barium enema to evaluate the entire colon should be performed. Barium enema might give an indication of colonic redundancy. Transit studies may be considered.

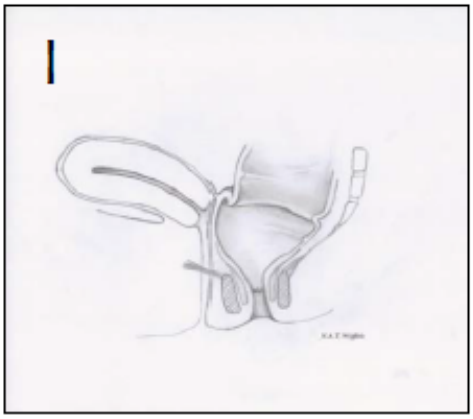
Video defaecography only if it is impossible to distinguish between IRP and ERP. In obvious full thickness prolapse it should not be necessary.

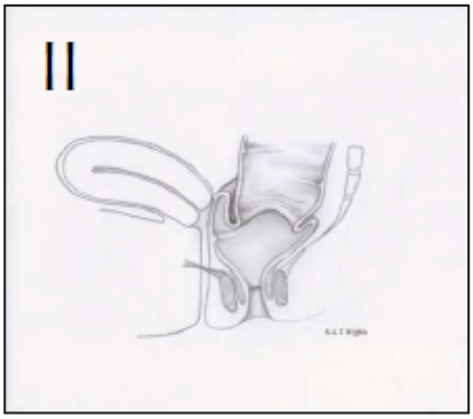
Evaluation of the sphincter complex by endo-anal ultrasound should be performed to indicate prognosis. Ulcer should be biopsied to exclude other pathology.

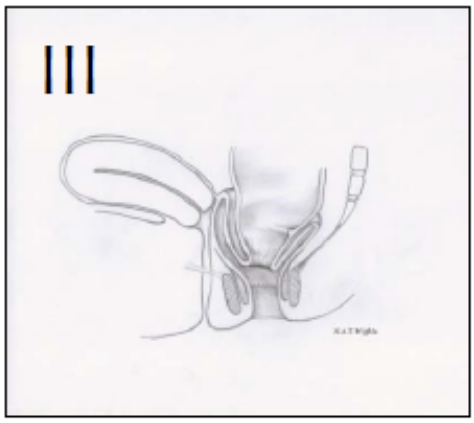
Oxford Rectal Prolapse Grading System

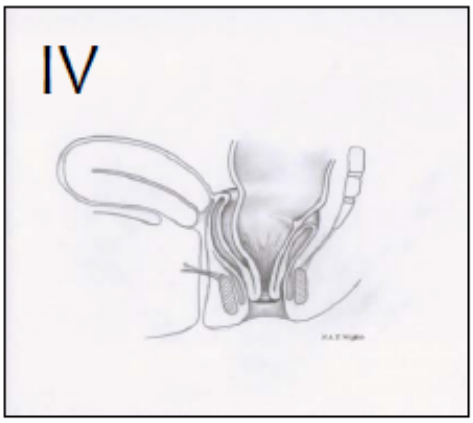
Developed at the Oxford Pelvic Floor Centre where it was shown that a significant reduction in maximal resting pressure was seen with Gr 3-5 prolapse. This is a radiological assessment with defaecogram.

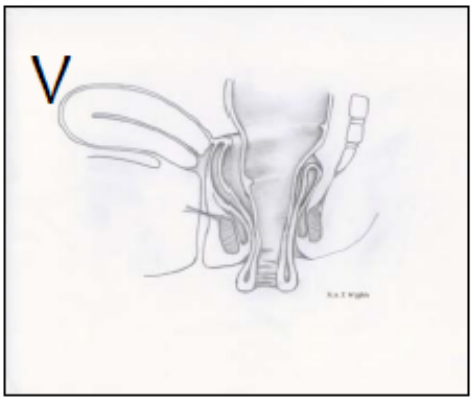
		Grade of Rectal Prolapse	Radiological characteristics of Rectal Prolapse
Internal (IRP)	*Recto-rectal Intussusception (RRI)*	I (high rectal)	Descends no lower than proximal limit of the rectocele.
		II (low rectal)	Descends into the level of the rectocele, but not onto sphincter/anal canal.
	Recto –anal Intussusception (RAI)	III (high anal)	Descends onto sphincter/anal canal.
		IV (low anal)	Descends into sphincter/anal canal.
External (ERP)	*External rectal prolapse (ERP)*	V (overt rectal prolapse)	Protrudes from anus.











Treatment

Acute

Gentle reduction should be attempted first and if necessary under anaesthesia. If the bowel viability is questionable urgent surgery is indicated.

Investigate, diagnose and the first line treatment for IRP is always first medical with thorough follow up.

Chronic

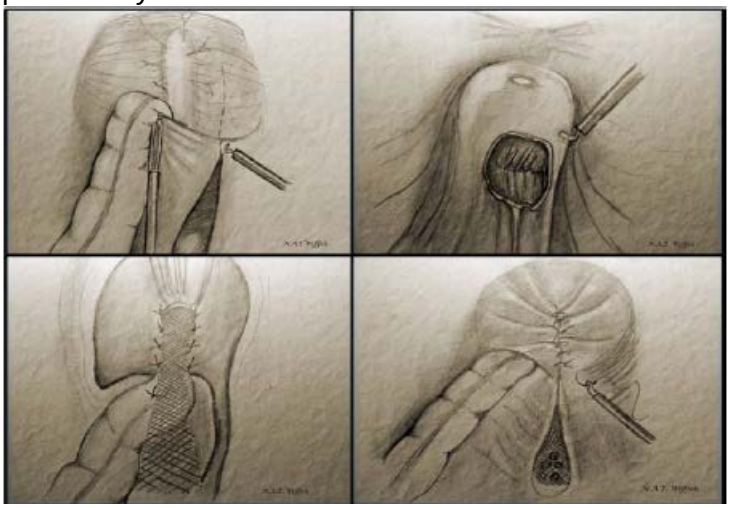
Surgical procedures in the management of prolapse can be divided in perineal and abdominal with the latter becoming more popular with laparoscopic approach. The basic decision regarding the more appropriate method is based on the patient characteristics such as age and comorbidities.

Reported recurrence rates are definitely lower with abdominal procedures but are marred by higher morbidity rates. Ventral rectopexy performed laparoscopically has

been reported to have a better functional outcome, attributed to avoidance of autonomic denervation by full rectal mobilisation as in Ripstein and Wells procedures[de Hoog DE, Heemskerk J, Nieman FH, van Gemert WG, Baeten CG, Bouvy ND. Recurrence and functional results after open versus conventional laparoscopic versus robot-assisted laparoscopic rectopexy for rectal prolapse: a case-control study. *Int J Colorectal Dis*. Oct 2009;24(10):1201-6].

Laparoscopic ventral rectopexy

The operation consists of four stages with fixation of polypropylene mesh and closure of peritoneal defect. The results are promising but no long term studies have been published yet.



In the final analysis the number of possible procedures indicates that the absolute ideal method for the management of rectal prolapse has not been found yet. A conclusion in a recent publication comparing abdominal (n=64) to perineal (n=40) procedures in a tertiary referral hospital over a 21 year period concluded that a higher overall recurrence rate was found in the perineal group[Lee JL, Yang SS, Park IJ et al. Comparison of abdominal and perineal procedures for complete rectal prolapse: an analysis of 104 patients. Ann Surg Treat Res. 2014 May;86:249-55.].

Carefully planned and executed surgery by way of preferred approach based on surgeon and patient characteristics is likely to yield the best outcome.

In my opinion the redundant portion of the colon should be excised with pexy of the rectum preferably with ventral mesh.

ETHICAL CHALLENGES IN PALLIATIVE SURGERY

David Cameron

"There are no definite criteria of who the surgeon should not operate on, but there are multiple clues as to who is unlikely to have a good outcome." Robert S Krouse (Department of Surgery, University of Arizona, USA).

Patients with advanced cancer present multiple technical and ethical challenges to the surgeon. With special reference to malignant bowel obstruction, some of the available evidence will be briefly reviewed together with non-surgical palliative options. Patients and their families need to understand the risks and benefits of any intervention especially with regards to the impact of surgery on quality of life and not just on length of survival. Suggestions will be made regarding effective and ethically sound communication strategies.

ELECTIVE SURGERY: CAN IT EVER BE UNETHICAL.
By Dr. B Bebington.

Biomedical Ethics frames the behaviour of clinicians; it does not define these activities' legality. The history of this aspect of our lives has a long and colourful past which pre-dates Hippocrates but which finds its earliest significant expression in his ideas. Ethics is all about the morality of behaviour and, in this day and age, could be defined in the following points:

1. Beneficence – The clinician has to, at all times, do good. The patient's best interest must be his primary concern in all instances. Not only this, in dealing with colleagues and the community as a whole his behaviour should only be for good. Contact at work should also be carried out with compassion, humility and dignity. There should be no inappropriate aggression in his dealing with patients or colleagues.
2. Non-maleficence – All activities must be carried out without harm; whether this be deliberate or accidental. Deliberation over every action is therefore necessary, with the objective to avoid harm and to achieve benefit. This should be applied to his colleagues and community.
3. Provision of the clinician's greatest skill should, on an ongoing basis, be his primary goal. All efforts must be made to give the patient the best medical care available at the time of the interaction. This means the clinician must keep abreast with the ever changing dictum of best practice. Peer review of his/her work, on an ongoing basis, should be part of daily practice. Criticism of past action should be given and taken as a benefit to his patient and practice; it should not be seen as a slight on his/her overinflated opinion of self.
4. The letter of the law must be upheld at all times. This includes respecting without prejudice the rights and dignity of all with whom he/she comes in contact. As a community leader, the doctor should strive to affect policy and institutional structure so as to benefit his patient.
5. The clinician has a duty to ensure that the best service is given to all in his community without bias. This may be difficult within the context of the society in which he/she lives but, on an ongoing basis, equality in resource allocation needs to be sought.

Within these basic guidelines the morality of the surgeon's behaviour in provision of elective surgery will be discussed. This will be didactic and broadly based. In preparation I recommend one read the witty and insightful work on this subject of Dr. Moshe Shein. I look forward to a lively debate!

END-OF-LIFE: AN ETHICAL CHALLENGE?
Prof Magda Slabbert UNISA

In an article published in *The Guardian* in July 2014, Desmond Tutu asks the question: "… why is a life that is ending being prolonged? Why is money being spent in this way? It could be better spent on a mother giving birth to a baby, or an organ transplant needed by a young person." He also refers to a study done where doctors confessed they had difficulty discussing end-of-life care with patients Tutu then remarks: "Physicians were once healers of life and easers of death but in the 20th century the training for the latter has been neglected".[29]

The duty to help is the moral basis in medicine. According to the WHO, palliative care neither hastens nor postpones death. Concerning the position in South Africa the Law Commission's Project 86 published in 1997[30] describes palliative care as medical intervention not intended to cure but to alleviate the suffering, including the emotional suffering of the patient. Such a patient could be one with terminal cancer. Generally these patients' lives are prolonged in comparison with the natural condition, by for example intravenous or nasogastric feeding, the administering of antibiotics to avoid or fight secondary infections and the administering of oxygen when necessary. It can happen that such a patient may find the situation unbearable as a result of pain and suffering or because the indignity of the situation. When the patient then requests the withdrawal of assistance practitioners sometimes assume that patients are behaving irrationally and are thus incapable of giving informed consent. The right to refuse medical treatment where the patient has the necessary mental capacity is acknowledged in our law. The only requirement is that the patient should be fully informed with regard to the consequences of his refusal. He should also understand the nature of the consequences. Our courts acknowledges the medical practitioner's obligation to comply with such a request and that, in doing so, he or she would not act unlawfully, either according to criminal law or in terms of private law, even if such an action would have the effect of hastening death. Some medical practitioners however, seem to be under the misconception that it is their duty to prolong life at all costs, notwithstanding the quality thereof and they may even influence the patient, or his family to continue the life-prolonging treatment. In palliative care some medical practitioners will even fail to supply pain-killers to ensure effective relief of pain for the patient, as they are afraid that they may be criminally prosecuted on account of the fact that such a large dosage of pain-killers may hasten death and that they may therefore be held criminally liable on the basis of *dolus eventualis*.

The truth is actually that the administering of drugs to a terminally ill patient would be lawful, even if it has the secondary effect of hastening death BUT only if the doctor acted in good faith and used the normal drugs in reasonable quantities with the object of relieving pain and without the intention of causing death. The administration of pain killers must not be defined according to side-effects, for example the shortening of life, but according to its aims which is to combat the pain of which the patient is suffering. The doctor's intention, and the evaluation of the pain and distress suffered by the patient, is of crucial significance in judging the double effect. (*S v Hartmann* 1975 (3) SA 532 (C)). An Indian doctor of New Delhi wrote in an article on ethics in palliative care:

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[29] http://www.dignitysa.org/blog/ [Accessed 9 September 2014].
[30] South African Law Commission, Discussion paper 71, Project 86 "Euthanasia and the artificial preservation of life" 1997.

> "We had a patient with lung cancer who suffered from breathing difficulty and pain; he was constantly breathless, could not lie down, and did not sleep for nights together. Morphine calmed him down; he felt relieved, could sleep soundly, and passed away peacefully after two weeks. His wife felt a sense of relief when he could sleep well."[31]

End-of-life care is both a medical and an ethical challenge. An ethical problem arises in any situation in which the wellbeing and interests of people are in conflict. Ethics is therefore a balancing act – it is the process by which one decides how to balance the interests of the various stakeholders. Making an ethical choice means that we must:

1. Be able to identify the various **stakeholder interests**, that is the interest of ALL parties who might be influenced by the decision that is being made
2. Balance these interests in a way that complies with certain ethical norms and values such as fairness, honesty, transparency etc.

When faced by an ethical dilemma like administering pain killers with the double effect, apply a **DECA** method:[32]

> **Describe** – describe the problem, whose interests are at stake, what are the possible solutions.
> **Evaluate** – evaluate the ethical problem and possible solution by using, deontology, teleology (utilitarianism), virtue ethics, beneficence, non-maleficence, justice, autonomy and dignity.
> **Consult** – consult others; the families, colleagues, HPCSA guidelines, spiritual leaders etc.
> **Act**.

Ethics is not intuition but a rational evaluation of the context through following a rational process.

Desmond Tutu refers to the case of Craig Schonegevel. After 28 years of struggling with neurofibromatosis, and no help to assist him with dying, he decided to take his own life. He swallowed 12 sleeping pills, put two plastic bags over his head tied with elastic bands and was found dead by his parents the next morning. Craig wanted to end his life legally assisted, listening to his favourite music and in the embrace of his parents. Our legal system denied him and his family this dignity. Tutu then remarks that some say palliative care, including the giving of sedation to ensure freedom from pain, should be enough for the journeying towards an easeful death. Other opine that with good palliative care there is no need for assisted dying, no need for people to request to be legally given a lethal dose of medication. Some also argue on the basis of the right to autonomy that they would like to die conscious of what is happening instead of in the fog of sedation, they want to be alert and truly present with loved ones when the end has come.

The sanctity of life should be respected – but not at any cost.

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[31] Mohanti B K "Ethics in Palliative Care" http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2902121/eport=printable [Accessed 27 June 2014].
[32] *Theoretical and Applied Ethics,* only study guide for PLS3701 Unisa.